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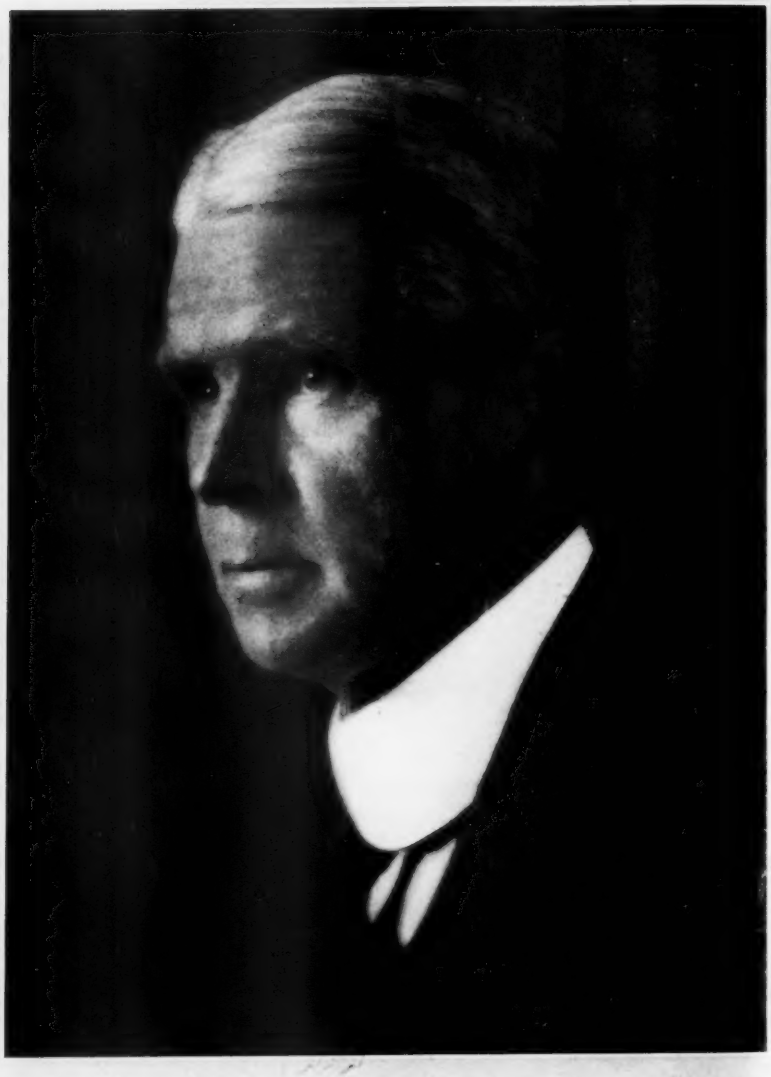

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L. Emmett Holt.

OBITUARY

LUTHER EMMETT HOLT, M.D.

Dr. Luther Emmett Holt died of myocarditis on Jan. 14, 1924, in Pekin, China, where he had gone to give a course of lectures in the Pekin Union Medical College. Thus passed away the dominant figure in American Pediatrics.

Dr. Holt was born in Webster, New York, on March 4, 1855, the youngest son of Horace and Sabrah Curtice Holt. He received his undergraduate education at the University of Rochester, and after graduation in 1875, taught for a year at the Riverside Institute in Wellsville, New York. He studied at the Buffalo Medical College but received his degree from the College of Physicians and Surgeons (Columbia University) in 1880, and was appointed to an internship in Bellevue Hospital.

It was the fortunate and sympathetic association with Dr. Virgil P. Gibney during his medical school period that drew Dr. Holt toward the problems of disease in children, and thus directed the activities of the rest of his life. He served for many months as a student assistant in the Hospital for Ruptured and Crippled where Dr. Gibney was the chief surgeon, assisting in the endless duties of an active hospital. So much was he influenced by the interests thus formed that, as soon as he left Bellevue Hospital, he entered eagerly on the task of acquiring a broad knowledge of the diseases of infancy and childhood, then no easy task. Hospitals for children were usually designed primarily for orthopedic and surgical diseases, and in those where there were medical services these were discontinuous and insufficiently provided with assistants and facilities. It was, therefore, necessary for one who would be continuously at work, and such was always Dr. Holt's habit, to be connected with a number of institutions whose services would dovetail. So it was that he was on the staff of the following institutions, each for a number of years: The Northwestern Dispensary, the New York Infant Asylum, the New York Foundling Hospital and the Nursery and Child's Hospital. It was in the Babies' Hospital, however, with which he was intimately associated from 1889 until his death, that his chief clinical work was done. For many years he was the physician-in-chief. The growth of this institution was the result of his guiding hand. The Babies' Hospital began by occupying a dwelling house on Lexington Avenue. It grew to a large modern building with excellent equipment, while the medical studies that emanated from it gave to the hospital a world wide reputation.

Dr. Holt's contributions to medicine began early and continued uninterruptedly until his death. They embraced many aspects of pediatrics and were founded on a thorough pathologic knowledge. The most important related to the diseases of infancy and early childhood, which was always the field of his chief interest and occupation.

It was as a teacher that Dr. Holt was preeminent. He instructed undergraduates, and by his books and writings he taught the whole medical profession of this country. He was professor of diseases of children at the New York Polyclinic Hospital from 1890 to 1901, when he resigned to become Carpentier Professor of Diseases of Children at the College of Physicians and Surgeons (Columbia University) in succession to Abraham Jacobi. This professorship he held for twenty years. His success as a teacher depended on many things, an earnest desire to impart knowledge, an infinite capacity for taking pains, a clarity of thought that made complicated questions appear plain and a simplicity of exposition that could hardly be equaled. The same qualities appeared in his writings. Small wonder then, that the ears of his listeners and the eyes of his readers were many.

That Dr. Holt possessed the ability to think clearly and advise wisely was widely recognized. As a result, he was called on to play a major part in the development of important projects. He was one of the original board of directors of the Rockefeller Institute and was its secretary until his death. He gave much time and thought to the New York Academy of Medicine, and he was an editor of the AMERICAN JOURNAL OF DISEASES OF CHILDREN for more than ten years. Twice he was president of the American Pediatric Society. On resigning his chair at the College of Physicians and Surgeons he devoted an increasing amount of energy and thought to the American Child Health Association, of which he was first vice president. Attempts to prevent disease and death among children had always appealed to him and, when it became possible for him, he threw himself with the enthusiasm of youth and the wisdom of age into what seemed to him a veritable crusade for the betterment of the health of the young.

Dr. Holt was a trustee of the University of Rochester, and the recipient of many honors from institutions and learned societies. The world recognizes his accomplishments and regrets the loss of one who unselfishly has done so much for the public good. Those who knew him intimately have a keen, personal sorrow. He was to them a sincere, undemonstrative friend, revealing the warmth of his feeling by generous, unsolicited acts of kindness. One could not but recognize that he was honest and loyal to the core. There naturally followed admiration and affection. It was impossible to believe that there was anyone more worthy of trust. In the minds and hearts of many his memory will long remain.

John Howland.

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ATONIC INSUFFICIENCY OF THE STOMACH A CAUSE OF VOMITING AND OF LACK OF APPETITE IN INFANTS*

GUSTAF LINDBERG, M.D.

NORRKÖPING, SWEDEN

Severe vomiting, endangering the development and even the life of the infant through the continuous loss of food, is most frequently met with in the new-born and during the first weeks of life. The cause of this vomiting may be a congenital stenosis or atresia of the intestinal canal, or more commonly a pylorospasm or a pyloric hypertrophy with stenosis. Less alarming cases of vomiting are also more frequently seen during the first period of life than later. While the causes already mentioned are fairly well recognized, the etiology of this milder type of vomiting remains rather obscure; and now and then one observes cases in which severe vomiting is due to none of the conditions mentioned. Some observations that seem to throw light on this particular point will be reported in this paper.

The type of vomiting I refer to is usually called habitual vomiting. Among the causes suggested, usually in a rather vague way, I mention aerophagy. The swallowed air is supposed to cause an explosive emptying of the stomach through the cardia. An abnormal sensitivity of the mucous membrane has also been considered a cause, particular emphasis being given to a neuropathic constitution. All of these cases, as is generally recognized, show no peristalsis of the stomach, and no pyloric tumor can be palpated.

I have observed several cases where another mechanism was responsible for the vomiting and here report a typical instance.

REPORT OF CASE

E. B., a full-term baby girl, with an initial weight of 3,400 gm., born of healthy parents, but a nervous mother, and who nursed energetically, started to vomit after two days. The vomiting, not very marked at the beginning, gradually became more frequent and voluminous. It occurred after the meal or after a short interval, and was for the most part not projectile. In spite of decreasing weight, the general condition remained rather satisfactory for some days. At the beginning of the second week, the weight dropped more rapidly, and there was loss of appetite. The baby vomited after every meal and frequently also a long time after the meal. The vomiting was now

* Received for publication, Sept. 10, 1923.

* From the pediatric service of Norrköping City Hospital.

voluminous and projectile. The temperature was subnormal, and the baby was rather dull. The vomited material was often yellowish. The stools were soft, yellow and scanty.

I saw the baby for the first time two weeks after birth. The general condition was poor; the eyes were sunken, and the skin was inelastic and slightly icteroid. There was marked drowsiness. The heart and lungs showed no abnormal signs. The upper left quarter of the abdomen was slightly distended. Here a distinct peristalsis of the stomach was seen, with waves starting far

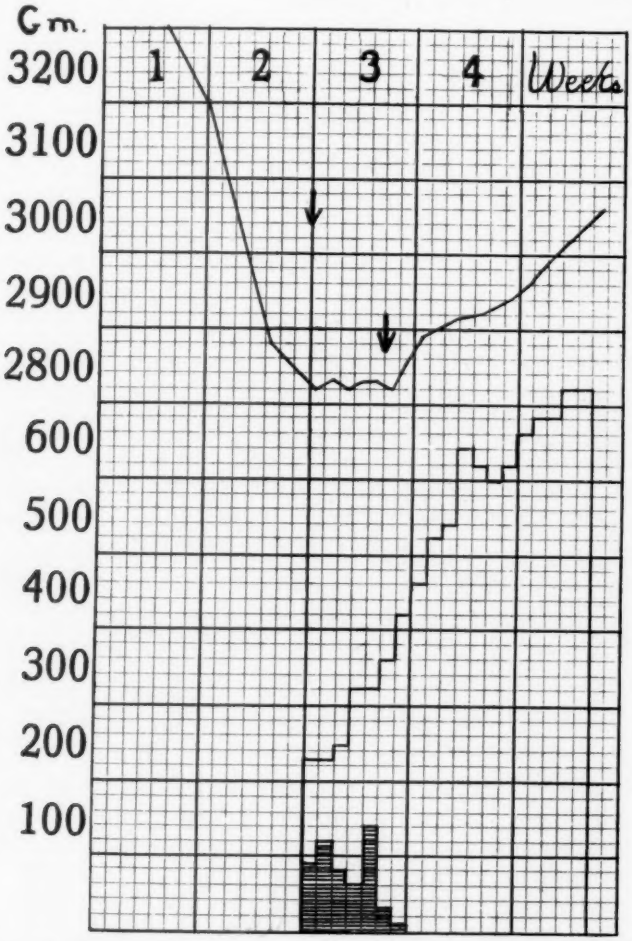

Fig. 1.—The upper curve represents the weight. The first arrow indicates the day when the hypodermic Ringer injections were started. The second arrow indicates when the Ringer injections were discontinued and the new therapy, with the baby in the vertical position, was introduced. The lower curve represents the amount of milk taken in twenty-four hours. The shaded area represents the amount of milk vomited in twenty-four hours.

to the left and progressing up to the midline, but not extending beyond. On percussion of the abdomen, vomiting readily occurred and the distension entirely disappeared. Owing to its serious condition, the baby was transferred to the

hospital. Weight at admission was 2,800 gm. The general condition was unchanged. The baby was nursed eight times a day as it had been while at home. To prevent further drop in weight, a hypodermic injection of 100 c.c. of Ringer solution was given daily. Figure 1 charts the course in the hospital. The first arrow indicates the day of admission. The appetite was very poor, only 200 to 300 c.c. a day being taken in eight meals, at the age of 2 weeks, although there was a plentiful supply of breast milk. About half the milk taken was vomited, and the baby was in a severe state of starvation.

By the administration of Ringer's solution, it was possible to prevent further loss of weight, but at the same time it was evident that we had to do with a

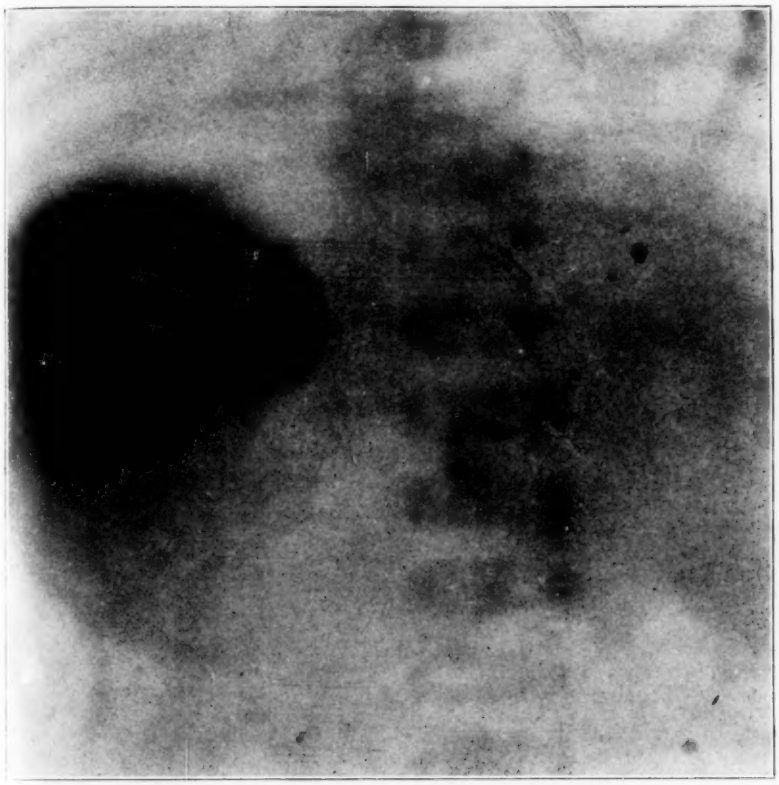

Fig. 2.—Roentgenograms taken with child in horizontal position, 100 gm. of breast-milk and 5 gm. of "contrast powder" having been introduced. The stomach does not empty.

serious condition, and the prognosis was considered doubtful. The diagnosis of pylorospasm was of course considered, but against this diagnosis stood the fact that the vomited stomach content sometimes showed a discoloration due to bile. Trials with papaverin and atropin proved unsuccessful in this case, as in numerous others.

To reach a definite diagnosis, the function of the stomach was studied under the fluoroscope, with an unexpected result. The examination was made in the morning, on an empty stomach. Through a fine catheter, 100 c.c. of breast

milk mixed with 5 gm. of "contrast powder" was introduced into the stomach. This was done with the patient lying down, and the behavior of the stomach was observed every five minutes.

As shown in Figure 2, none of the stomach contents passed through the pylorus as long as the baby remained in the horizontal position. In correspondence with the distension visible on the abdominal wall, the stomach contents had accumulated to the left of the vertebral column. In spite of clearly visible peristalsis, nothing was passed on through the pylorus. Peristaltic waves occurred now and then, but there were no signs of a tonic contraction of the stomach around its contents. This condition of insufficiency lasted as long as the baby remained in this position.

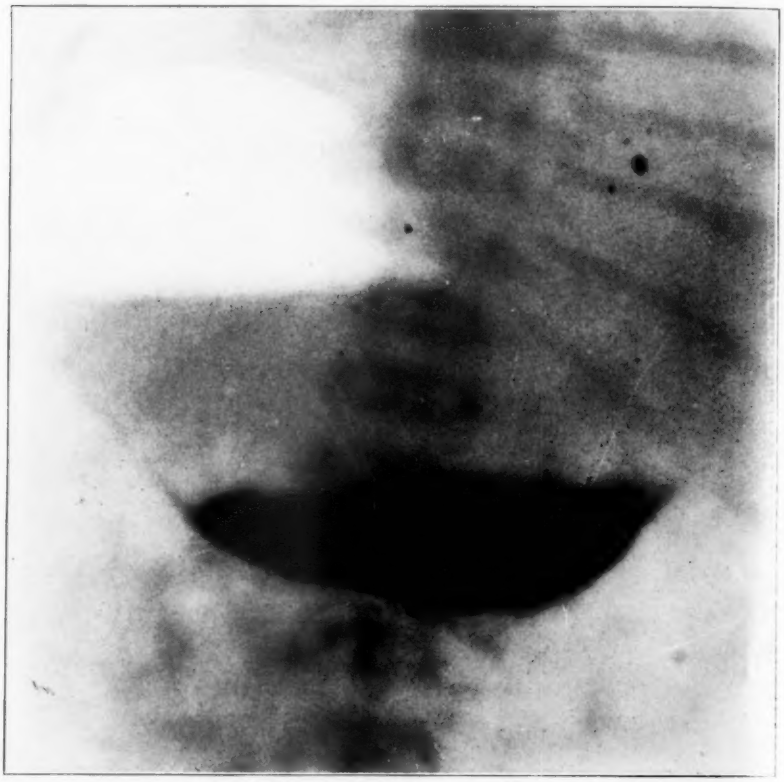

Fig. 3.—Roentgenogram taken with child in vertical position. The emptying of the stomach into the duodenum and the jejunum starts at once.

The observations were continued with the baby in the vertical position. The surprising fact was then immediately brought out that, as soon as the position was changed, the stomach contents at once started to pass over into the duodenum, and abundantly (Fig. 3). Even in this new position, there was a complete absence of tonic contraction, only a moderate peristalsis with big waves being seen. In the vertical position, the stomach now emptied rapidly, so that, after fifteen minutes, large amounts of the contrast meal were seen low down in the small intestine.

Since it had thus been proved by the roentgen-ray examination that no pyloric or other kind of obstruction prevented the emptying of the stomach, and

it also was clear that the emptying took place in a vertical but not in a horizontal position, the baby was fixed almost upright in the bed by the aid of pillows and a strap around the chest and underneath the arms. The day for this change is designated in Figure 1 by the second arrow. The rest of the curve demonstrates the correctness of the conclusion drawn from the roentgen-ray examination. The vomiting completely disappeared at once, and a rapid growth in weight set in, in spite of the discontinuance of the Ringer injections. This improvement continued steadily, the appetite increased at once and no vomiting occurred unless the baby was lowered to a horizontal position. After three weeks, the baby could lie down without vomiting, and later development was normal.

To understand the pathogenesis of the clinical picture described, it is necessary to know the function of the stomach in the baby, as this function has been made known to us by earlier roentgen-ray studies. As Groedel first pointed out, the stomach in the adult possesses a double function. First, it has a tonic function, the walls of the stomach contracting around its contents, giving to the stomach a varying volume and shape according to the degree of fulness. Stiller called this the peristolic function, this name having been generally accepted. The second function is the peristalsis, consisting of waves of contraction progressing from the cardia toward the pylorus. The emptying of the stomach occurs through the joint peristolic and peristaltic action. The stomach of a normal infant differs from the stomach of an adult both in shape and in function, as was brought out by the first roentgen-ray studies on the subject. Thus, Leven and Barrett showed that the stomach of the infant does not contract around its contents, which means the peristolic function is not developed. This has been confirmed by later investigators, Flesch-Peteri,[1] Epstein [2] and others. The peristaltic function occurs as in adults and is, as a rule, sufficient for the satisfactory emptying of the stomach. Because of the absence of the peristolic function, the infant's stomach is like a flaccid balloon, changing shape and position according to the amount of its contents and the position of the baby. It remains completely distended, having only a small content, and a large "stomach bladder" is normal in the infant. Further, it was observed by Flesch-Peteri that the absence of a peristolic function depends on the nature of the content. If the milk is replaced by food of more solid consistency, a powerful tonic contraction around the content occurs even in the infant. There seems, therefore, no difficulty in arousing the peristolic function, through

1. Flesch-Peteri: Magenuntersuchungen mittels Roentgenstrahlen im Saeugelingsalter, Ztschr. f. Kinderh. **2**, 1911.

2. Epstein, B.: Ueber die Beeinflussung des habituellen Erbrechens des Saeuglings durch Brei-Verfuetterung, Jahrb. f. Kinderh. **93**:360, 1920.

providing a sufficiently substantial stomach content. Epstein has confirmed this, and he has, like other investigators, both earlier and later, employed solid food in treating vomiting in infants.

Correlating these facts with the observations in the case here reported, there seems to be no doubt that the inability of the stomach to empty itself in a normal way when the baby was in a horizontal position was due to the absence of a proper peristolic function. This is confirmed by a successful outcome of the therapy indicated by the roentgen-ray examination. When the conditions for the emptying of the stomach were improved by the vertical position, the vomiting ceased. Trials with solid food were unsuccessful in this case; in similar cases, I have, however, found solid food useful.

At first, I was inclined to look on the case just reported as a mere oddity. But having had my attention drawn in this direction, observation of other cases of loss of appetite or vomiting in the new-born or young infants during the first weeks of life gradually made it clear to me that the cause was not infrequently the same as in the case described. In cases of vomiting without signs of pylorospasm or any other obstacle to the emptying of the stomach, I repeatedly observed the same therapeutic result from the use of the vertical position described. Infants with a persistent lack of appetite preventing any gain in weight showed an immediate improvement or complete recovery after the simple change from the horizontal position to the vertical one. These observations refer, however, to the first weeks of life only. I do not know whether the same mechanism can be the cause of vomiting and lack of appetite in older infants. But I consider it improbable that this type of insufficiency here plays any independent rôle. At least, I have always found a normal motor function of the stomach as soon as the infants have passed the first months. During or after any nutritional disorder in older bottle-fed babies, the atony of the stomach is a factor of recognized importance.

It seems interesting to correlate with the findings here presented the common practice of mothers in handling babies when they vomit. The manner of carrying the baby in a half-erect position, slowly rocking it back and forth, continued for some time after each meal, seems now rational enough and is undoubtedly of therapeutic value. This therapeutic effect has been explained as due to a diminution of the amount of air present in the stomach, the air being more easily expelled through the cardia. It is easy to observe that this is often the case. In the case described here, however, the "stomach bladder" seemed bigger in the vertical position than in the horizontal. The main benefit of carrying the babies in a more or less vertical position is, therefore, in all probability, an easier emptying of the stomach.

The peristalsis observed through the abdominal wall in the case described deserves particular attention; and this is not only from a theoretical point of view. At present, it is generally accepted [3] that a visible peristalsis occurs only in pylorospasm or pylorostenosis of some other origin. In my case, this is easily ruled out. On the screen, the pylorus was wide open, and the vomited material had been observed sometimes to be colored by duodenal contents. Nevertheless, peristaltic waves were repeatedly observed through the abdominal wall, sometimes quite marked. This proves that visible peristaltic waves are not pathognomonic for pylorostenosis, as has generally been considered. Because of the content of air and fluid, the anterior wall of the atonic stomach in my case was evidently quite close to the thin abdominal wall. Peristaltic waves may thus become visible without being any stronger than normal. This brings up the question as to whether some of the mild cases of "pylorospasm," in which the symptoms disappear as soon as small and repeated meals are given and the stomach perhaps has been washed out twice, are correctly diagnosed as pylorospasm, or rather belong to the type of tonic insufficiency here described. The majority of the cases of pylorospasm are, of course, of a more serious type, but in some cases treatment consisting in merely a change in position may be tried.

Finally, I wish to emphasize again that not only vomiting but also lack of appetite in the new-born may be due to this atonic condition, and may be tentatively treated accordingly.

CONCLUSIONS

1. At birth and during the first weeks of life, incomplete emptying of the stomach is not an uncommon finding.
2. The symptoms are vomiting or lack of appetite, or both.
3. The symptoms may disappear if the baby is kept in a half-erect position.
4. These cases may simulate a pylorospasm.
5. Peristalsis visible through the abdominal wall may sometimes be observed without pylorospasm or pylorostenosis being present.

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3. Finkelstein: Lehrbuch der Saeugelingskrankheiten, Ed. 2, Berlin, 1921.

GENITO-SUPRARENAL SYNDROME (SUPRARENAL VIRILISM) IN A GIRL ONE AND A HALF YEARS OLD, WITH SUCCESSFUL OPERATION *

ARTHUR COLLETT, M.D.

CHRISTIANIA, NORWAY

Hippocrates [1] described two cases of virilism in married women, whose bodies resembled the male's and were covered with hair. These women had a beard, and their voices were deep. Vesal describes similar cases. William Cooke (1756) was the first to give a more exact description of a case, in connection with a suprarenal gland tumor in a 7-year-old girl. She was enormously fat, with a thick growth of hair on the face and genital organs. Analogous observations have at times been made by many authors. Bevern and Romkild (1802) describe a 3½-year-old girl, who looked like a woman of 20, with a thick growth of hair on the genital organs and on the face.

Tilesius (1803) described a 4-year-old girl, enormously fat, with premature development of the breasts, and hair on the genital organs, and with a tumor the size of a goose egg in the left suprarenal gland. Bulloch and Sequeira [2] (1905) were the first to point out when describing a similar case in an 11-year-old girl, that the tumor develops in the suprarenal cortex. Bulloch and Sequeira further state that the other endocrine organs in the patient were normal, but they could not find the thymus. They have collected twelve cases of tumor of the suprarenal gland with sexual changes (inclusive of their own case) and thirteen cases without such changes, and with these cases as a basis give valuable assistance in making clear the connection between the tumors of the suprarenal glands and the sexual organs. Their conclusions will be mentioned later.

While Bullock and Sequeira, in their excellent treatment of the subject, restrict themselves to the condition of children. Bortz, in 1909,

* Received for publication, Oct. 31, 1923.

* From children's section of the State Hospital.

* The case was presented before the Norwegian Medical Association in Christiania, Oct. 27, 1920 (referred in the publications of the Association, 1920, p. 116), and at the second Northern Pediatrics Congress in Stockholm, June, 1921 (Congr. forh., p. 134), under the title "Hermaphrodism and Too Early Sex-Development in a One and One-Half Year Old Child."

1. The historical data are principally from Bulloch and Sequeira and Gallais, and from Biedl (Innere Secretion, 1916).

2. Bulloch and Sequeira: On the Relation of the Suprarenal Capsules to the Sexual Organs, Path. Soc. of London, 1905.

described the disease in adults. Neugebauer (1908) had already determined that suprarenal glands were enlarged in a number of pseudo hermaphrodites (of female mold externally).

Apert [3] (1910) collected thirty-five cases, with necropsy, in persons of all ages (none of his own observation) and showed clearly that all the different descriptions represent different types of the same disease, the manifestations of which change according to the age at which the disease develops, but the nature of which is always the same. Like Bulloch and Sequeira, Apert maintains that there is a special syndrome arising from the changes in the suprarenal cortex. He gives the following forms: (1) hyperepinephry (with hyperplasia of the cortex), with (*a*) a marked growth of beard, (*b*) excessive growth of fat tissue and (*c*) early development of the body, with disturbances of the genital functions (thirty-one cases); (2) hypo-epinephry (with hypoplasia of the cortex), with (*a*) scant growth of hair, (*b*) poor development of fat tissue and (*c*) underdevelopment of the body (four cases).

According to Apert, there are distinguishable five types of hyperepinephry, varying according to the age of the individual at the time of the appearance of the disease, but all with the three above-mentioned symptoms. Most of these symptoms are seen in women.

1. *Hyperepinephry of the Embryonal Period.*—Hyperepinephry in this early period results in the individual becoming a hermaphrodite, with internal female genital organs, but outwardly of masculine form, with undeveloped breasts; hypospadiac clitoris peniformis; vulva like a cul de sac; uterus and ovaries. There is marked hypertrophy of the suprarenal glands.

2. *Hyperepinephry of Fetal Period.*—The anomaly is less pronounced, but there is no doubt as to the sex. There is a large clitoris, the uterus and ovaries are atrophied, and hypertrichosis is present. The hyperplasia of the suprarenal gland probably dates from the later period of fetal life.

3. *Hyperepinephry of the Prepuberty Period.*—There is (*a*) abnormal body development, with pubertas precox; (*b*) adipositas; (*c*) hypertrichosis, and (*d*) partial hypertrophy of the clitoris.

4. *Hyperepinephry of Maturity.*—Menstruation stops, and marked adipositas and hypertrichosis are present.

5. *Hyperepinephry During the Period Near and After the Menopause.*—The clinical picture here is indistinct. There is marked adipositas, and of disturbances of the genital functions metrorrhagia, and not even hypertrichosis is present.

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3. Apert, E.: Dystrophies en relation avec des lésions de capsules surrénales, hirsutisme et progeria, Bull. Soc. de pédiat. de Paris **12**:501, 1910.

It is noticeable that the earlier the condition develops, the more marked are the changes.

Because the most constant symptom of hyperepinephry is hypertrichosis, Apert calls the disease hirsutism. The opposite condition is called by Gilford progeria (aged before time), and by Variot it is called "nanisme senile."

Alfred Gallais,[4] who has written a comprehensive treatise on the subject (1914), calls the clinical aspect produced by hypertrophy (physiologic or neoplastic) of the suprarenal gland "Le syndrome génito-surrénal."

This syndrome manifests itself, according to Gallais, in four forms: (1) le pseudo-hermaphrodisme surrénal (the disease occurs before birth); (2) le virilisme surrénal (the disease occurs after birth; the genital organs are formed); (3) la forme menstruelle; (4) la forme obstétricale.

The two last forms are characterized by E. Glynn[5] (1921) as superfluous and of doubtful justification.

If one reads the history of the disease, it is found that Gallais' cases are not always distinct. The first two forms correspond, as will be seen, to Apert's four forms.

Glynn prefers to classify all cases of abnormal sex character with tumor of the suprarenal gland under the name of suprarenal virilism. Since Apert's treatise, our knowledge of the symptoms and course of genitosuprarenal syndrome has been extended by a number of observations on individuals of all ages. Gallais, in 1914, refers to no less than fifty-one cases, among them four of his own observation. All of them were in women and children; reference is made to a doubtful case in a man. It thus appears that these tumors of the suprarenal gland do not cause sex changes in men.

At that time there were seventeen cases in children, collected by Glynn. Later one was observed by Tschernobrow[6] (in an 11-year-old boy); one by Schiff (in a 2-year-old girl), and one by Hijmans[7] (in a 3-year-old girl). These, with my case (in a 1½-year-old girl), total twenty-one cases, four of which were in boys.

There is no sex change seen in boys, but too early development, hypertrichosis and premature development of the outer genital organs, without potency. Sex power develops later, and slowly. In girls, menstruation does not appear early. Bulloch's and Sequeira's case,

4. Gallais, Alfred: Le syndrome génito-surrénal, Paris, 1914.

5. Glynn, E.: A Comparison Between Ovarian "Hypernephroma" and Luteoma and Suprarenal Hypernephroma, with Comments on Suprarenal Virilisme, J. Obst. & Gynec. Brit. Emp., 1921, p. 48.

6. Tschernobrow, E.: Ueber eine Geschwulst der Nebenniere bei einem 11 jährigen Knaben mit frühzeitger Geschlechtsentwicklung, Zürich, 1919.

7. Hijmans, cited by Glynn, Footnote 5.

in which it occurred at 9 ¾ years, is an exception. As a rule in this syndrome, there is a false pubertas precox, as only the secondary sex characters are developed prematurely. Illustrating the real pubertas precox is Craterus' case: An individual was, in the course of seven years, a child, a youth, an adult, a father and dead.

The marked development of the body may be manifested either as obesity or as great muscular development (l'enfant Hercule).

The hair growth in girls is most often of masculine type, but in the case of our patient the pubes were bounded horizontally, while the hair growth was otherwise even hypervirile. Ossification and dentition are often hastened. Thus, in the case of our patient, ossification corresponded to that of a 3-year-old child and the pelvis was of a masculine type. The development of the teeth was normal.

According to Leiner,[8] a child with the genitosuprarenal syndrome is dull and intellectually subnormal. On the contrary, our patient was lively and sensitive, with a mature expression. Hijman's 3-year-old girl was of similar type. In the most complete form of suprarenal virilism (with acquired lesion), Gallais claims that one can distinguish two phases in development. In the first phase, there is amenorrhea, sometimes accompanied by pains of the pelvis, nausea and vomiting. Adipositas, hyperasthenia, nervousness, strange mental phenomena are present and the sexual instinct deviates; the character is changed, and the patient becomes violent. There may appear crises of terror. Masculine hypertrichosis is constant; pigmentation, such as is shown in dirty gray spots on the forehead, in front of the armpits and on the back, forearms and the hand, is rare. In the second phase, there is emaciation, with red stripes on the abdomen, armpits, groins, etc.; progressive asthenia, and irradiating breast and loin pains. A tumor may be palpated in the abdomen. The patient may be without will power, and filled with suicidal thoughts.

ETIOLOGY AND PATHOGENESIS

The cause of tumor of the suprarenal gland is just as obscure as the cause of other tumors. As regards the suprarenal syndrome, Gallais states that in one case the patient's mother, in another case the patient's father, had died of tumor. Our patient's grandmother on the father's side had cancer of the breast. There are cases of nervousness in the family, as in our case, together with malformation from birth, as, for instance, hare-lip. As mentioned above, there has been no case reported in men; and in children, girls are far more frequently attacked than boys (17:4). With regard to localization of the tumors, it is agreed that tumors in the suprarenal *medulla* are never accompanied by changes

8. Leiner, J. H.: Pubertas Præcox with Especial Attention to Mentality, Endocrinology **4**:369 (July-Sept.) 1920.

in sex characteristics. These tumors are always situated in the cortex. They may arise partly from accessory suprarenal glands (these consist always of cortex substance) in the broad ligament (Bovin).

Cases of the syndrome with hypernephroma in the ovary are described by Debeyre and Riche (Gallais, p. 221), but Bovin [9] (1909) and Glynn [5] (1921) both hold that there has not yet been produced certain proof of the existence of real hypernephroma in either the ovary or the testis, but quite near to them and then most often in children. Of hypernephromas in the kidney, Glynn and Hewetson [10] say that they are quite different in structure from those in the suprarenal gland and are never accompanied by sex disturbances. Gallais states that changes in sex characteristics are found only in adenomatous hypertrophy, adenoma or malignant hypernephroma, but not in sarcoma. However, in Bulloch and Sequeira's statistics are found two cases of virilism with large-cell sarcoma in the suprarenal gland (Colcote, Fox's and Ritchie's). Bulloch and Sequeira, however, say of Ritchie's cases that from microscopic examination, the histogenesis of the tumor is difficult to decide, though the type is sarcomatous.

It appears from the observations both of these authors and of others that in any case, sarcoma only exceptionally produces the syndrome. On the other hand, adenoma or tumor of the carcinomatous type does not always produce sex changes (Brüchanow's case in a 14-months-old girl; Rupprecht's case in a 2 ½-year-old girl may be cited).

With regard to the manner in which hyperplasia of the suprarenal cortex and tumor respectively produces the genitosuprarenal syndrome, there prevail various hypotheses. It is commonly supposed to be due to a hyperactivity of the supposed physiologic function of the cortex, which should promote the growth of the body and development of the secondary sex characteristics (Bulloch and Sequeira, Neurath,[11] Glynn,[5] Falta [12] and others). There is by some supposed to be a pluriglandular disturbance. Thus, for example, the hyperfunction of the cortex may secondarily influence the ovary (Wiesel, Gallais); while Blanchard,[13] supported by Pierre Marie [14] sees the cause exclusively in the disturbances in the sex gland. One more theory (Krabbe) [15] supposes that the appearance of the disease is due to the fact that the tumor develops from sex gland cells of masculine type, which early in the life

9. Bovin: Nord. med. Arch. **41**:4, Part 1, No. 15, 1908.
10. Glynn, E., and Hewetson, J. T.: J. Pathol. & Bacteriol. **18**:81, 1913-1914.
11. Neurath: Die vorzeitige Geschlechtsentwicklung, Ergebn. d. inn. Med., No. 4, 1909.
12. Falta: Die Erkrankungen der Blutdrüsen, 1913.
13. Blanchard, R.: Bull. de l'Acad. de méd., Paris **76**:47 (July 18) 1916.
14. Pierre Marie, quoted by Blanchard, Footnote 13.
15. Krabbe, K. H.: The Relation Between the Adrenal Cortex and Sexual Development, New York M. J. **114**:4 (July 6) 1921.

of the embryo have been involved in the suprarenal gland cortex. The possibility of such a displacement of the sex gland cells has been pointed out by Bulloch and Sequeira. Krabbe's theory will again be referred to.

Both the proximity of the germ of the suprarenal cortex to the germ of the sex gland, and certain physiologic conditions, indicate a near relationship between the functions of these organs. The suprarenal gland cortex and the sex gland both arise in the celomicepithelium, where the germs are closely associated, without any sharp boundaries, even intermingling, in part (Brachet,[16] p. 556). The relation, according to Soulié, is at an earlier stage so intimate that it is impossible to distinguish the tissues from each other.

Meckel (1806) thought that a functional connection between the two organs could be noted, as he found extremely well developed sex organs and very large suprarenal glands in guinea-pigs, and Nagel found similar conditions. The latter proved that, in birds and amphibious creatures, the suprarenal glands are swollen during the rutting season. According to W. Kolmer, the structure of the suprarenal gland cortex varies in guinea-pigs according to sex, age and the condition of the genital organs, so that one can actually speak of a secondary sex character in the suprarenal gland. In the female of this species, according to the same author, there occur cyclic changes in the suprarenal gland parallel with the functions of the genital organs. There is supposed to have been observed a compensatory hypertrophy of the suprarenal gland, especially of the cortex after double castration (Théodossief, Ciuccio). The remaining aspects of the supposed functions of the suprarenal gland will not be further discussed here, but it should be noted that the whole physiology of the cortex is still *sub judice*.

Even Gallais made reservations as regards the physiologic function of the cortex because of the influence of the tumor on the sex character; while Krabbe disregards the theory of the tumor's influence as a cortex hypersecretion. "Why should such produce a masculine puberty in girls and not a feminine one?" This characteristic influence must, according to Krabbe, be explained in quite another way. He supposes, in support of his interesting theory, that while the testis is developed almost directly from the original undifferentiated germ of the sex glands, the ovary passes through a stage wherein its cortex is feminine, while the medullary is testicular; a consideration which is founded on investigations of Laulanié, among others, and confirmed by a number of authorities, among them A. Kohn and Brachet.[16]

It is precisely this medullary, testicular part of the ovary which, at an early stage, is closely connected with the suprarenal gland cortex and

16. Brachet. A.: Traité d'Embryologie des Vertébrés, Paris, Masson & Cie, 1921.

which, according to Krabbe, should be involved in the suprarenal gland cortex during further development. Hypernephroma in girls with virilism are supposed by him to be produced from these testicular cells, and that through secretion of the testicular hormones masculation is produced. In a similar way, the hypernephroma developing in boys from displaced testicular cells cause too early sex development. Krabbe's theory agrees well with Conheim's theory about the development of tumors from displaced cells. It may be of interest in this connection to quote (p. 558) the embryologist A. Brachet in regard to the functional connection between the suprarenal gland cortex and the sex glands: "Not only are physiologic relations proved, but, with due regard for what the future may show, one may even question whether the proliferations of the germinal epithelium and of the interrenal ridge are not in reality one and the same formation, the destiny of which is determined by the symbiosis established between it and elements derived from another source—a symbiosis with gonocytes on the one hand and chromaffin cells on the other." (Les connexions physiologiques ne sont nullement démontrés mais, toutes réserves faites sur ce que réserve l'avenir on peut se demander si les proliférations de l'épithélium germinatif et de la bandelette interrénale ne sont pas en réalité, une et même formation dont la destinée est déterminée par la nature de la symbiose qui s'établit entre elle et des éléments issus d'autre source: Symbiose avec gonocytes d'une part, avec les cellules phaéchromes de l'autre.)

During a tour in West Norway in the summer of 1920, I had an opportunity to examine a child of extraordinary appearance. With the cooperation of Prof. Axel Johannessen, I obtained permission to place the child in the state hospital, Christiania, children's ward, so that further investigations could be made.

REPORT OF CASE

History.—M. E. M., born March 18, 1919, admitted to the hospital Sept. 8, 1920, discharged Oct. 30, 1920, was of a healthy family. There was some nervous affliction on the father's side, and the paternal grandmother had cancer of the breast. Both father and mother were healthy and well built, of medium height, good appearance and very intelligent. The mother had a rather deep voice. There had been no abnormities, such as that of the patient, in the family. The patient was the youngest of five brothers and sisters, all healthy and normal. Pregnancy was normal. The mother, in the third month, fell over a 30-foot precipice, with a horse and cart. She escaped with a fright. The child weighed at birth 5,000 gm. (the weight of all the brothers and sisters at birth was about the same), and had grown steadily. She was breast fed for four or five months. Later, little by little, cow's milk, porridge, vegetables and fish were given her. She had been healthy except that in December, 1919, at 9 months of age, she developed whooping-cough. In February, 1920, she had severe bronchitis with convulsions. So far as the parents could remember, an abnormal growth of hair on the genital organs began before the whooping-cough, at from 6 to 8 months of age; but not until after the bronchitis had the

growth of hair become thicker and extended over the trunk and extremities, just as the voice took on a deep rough sound, while before it was childish and clear. She gradually became heavy and fat, with bulging cheeks. She had been lively and not backward in mental development; on the contrary, the mother thought she was far quicker and cleverer than the other children were at a corresponding age. She could not yet walk or stand. The first teeth came at 5 or 6 months, as in the case of her brothers and sisters. It had been difficult to keep the skin free from roughness, and the cheeks had constantly been red and sore.

The parents had not noticed any abnormity in the form of the sexual organs. Bleeding from the genital organs had not been observed.

Examination.—The weight on admission was 15.10 kg. average (Camerer, 11.45 kg.; Holt, 10.68); the height, 80.75 cm. (Camerer, 79 cm.; Holt, 75.6);

Fig. 1.—Appearance of patient.

breast circumference, 53.5 cm. (Holt, 45.9); circumference of abdomen, 62.5 cm.; height, sitting, 50.5 cm.; head circumference, 49 cm. (Holt, 45.9). The child was heavily and plumply built, with a rather large head (Fig. 1). The face especially was bulging with fat; the cheeks were baggy. The ears were well-formed. The eyes had a clear, intelligent expression, too mature and sad. The back of the eye was normal; there was no stasis of the papilla (eye-section of the hospital). The voice was deep and somewhat rough, often rising to a squeak, as in the case of a boy at the time of change of voice.

By indirect laryngoscopy (Prof. V. Uchermann), it was seen that the vocal chords were unusually long and broad, almost as in an adult man. They were whitish, without essential injection, and closed well. No tumor was found. The

neck was short and thick; the trunk was large in all dimensions; the extremities were short and thick, especially the thighs. The hands and feet were somewhat large, but well formed. The skin, except for the face, was soft and elastic, with strongly developed panniculus adiposus. On the cheeks, the skin was much reddened and sore, with a few short hairs. There was no abnormal pigmentation. There was a marked growth of hair on the labia majora and mons veneris, with a horizontal boundary above (Fig. 2). The hairs were up to 3.5 cm. long. On the thighs, shoulders and back, and partly on the front of the trunk, there was seen a dark growth of hair up to 1.5 cm. long. There was no axillary hair.

Genitalia: The labia majora and mons veneris were well developed. In place of the clitoris, there was a penis-like organ about 1.5 cm. long (Fig. 3). It was covered on the front by a prepuce, which extended into the labia minora. When the prepuce was drawn back, there was seen a quite well-developed gland with corona in which there was plenty of sebum. There was no urethral opening on the peniculus, but on the under side there was a longitudinal furrow. The corpora cavernosa urethrae could be felt. There was some degree of volume change.

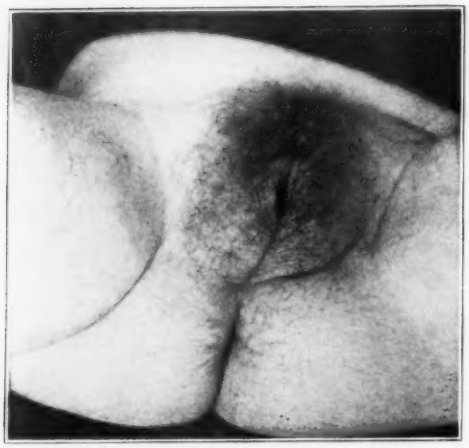

Fig. 2.—Growth of hair on genitalia.

Fig. 3.—Development of genitalia.

The urethral orifice was found in the usual place. Catheters were easily passed into the bladder. The hymen was normal and the vagina was about 5 or 6 cm. deep. By means of the speculum, the portio of the uterus, with normal orifice, was seen.

Through the rectum, the uterus was felt. Its length was about 3 or 4 cm., the breadth 1 cm. The thickness of the organ was normal. No prostate could be felt, nor adexa. There was no indication of mammary glands. There were a number of small lymphatic glands on the neck.

No abnormality of the thymus and thyroid could be noted, and the sella turcica, under roentgen rays, seemed normal. In the throat and heart there was nothing of note. In the lungs, there was the sound indicative of bronchitis. The abdomen was large, with a small umbilical hernia. The liver reached three fingers' breadth in front of the costal arch; the spleen could not be felt. Because of the clinical picture, we now sought for a suprarenal gland tumor. The right kidney was palpable but seemed normal. Under the left arch

of the ribs, we thought we could feel a tumor connected with the kidney. The surgeon, Dr. Backer-Gröndahl, confirmed this finding, and gave the following description of the condition: In the deep part under the left arch of the ribs a tumor with slightly knotted or rather twined surface was felt. Especially noticeable was a curling projection, the size of an almond. The boundary above could not be reached; laterally, it seemed the boundary was somewhat evenly bent and longitudinal. Downward it had a comparatively sharp side, extending a little from above and from the outside inward and downward to the quite palpable knot, which likewise formed a downward point. The tumor extended down until it was level with the point of the costa. It lay rather deep, but was not ballotable, as the hand could not reach high enough up at the back. Below this tumor, under a lower boundary, was felt another body which lay somewhat deeper, had a smooth slippery front and a smooth outward-bent side, and ended downward in an arch. The consistency and form reminded one of a kidney, about 4 or 5 cm. long, whose upper one third loses itself under the tumor. This was not ballotable, as it seemed to lie a little too centrally. None of the tumors were moved by the respiration. They could be pushed up and down a little. There was no soreness.

Bones: The head bones were firm; the fontanel was closed, and there was no raising of the epiphyses and no swelling of the ribs. There were sixteen

Fig. 4.—Appearance of tumor.

teeth. The pelvis measurement, interspinal, was 14.5 cm., intercistal, 15.5 cm.; that is, a masculine type. The roentgenogram of the wrist showed that it corresponds to the wrist of a 3-year-old child. The body functions were normal; the temperature was normal. In the urine, which was as clear as water, there were no abnormal ingredients.

Blood: The blood test revealed (Sahli 71): polymorphonuclear neutrophils, 33 per cent.; small lymphocytes, 48.33; large lymphocytes, 5.67; large mononuclears, 10.8; eosinophils, 2.67; mast cells, 0.33. There was nothing of note in the red blood corpuscles (L. Dedichen).

When, as in the present case, abnormal hair growth, marked body development and premature development of the secondary sex characters are associated, one must bear in mind the pathologic function of three organs; namely, the pineal gland, the sex glands and the suprarenal cortex. A disfunctioning of the pineal gland is due mostly to a growth, as a rule teratoma. Our patient, however, offered no sign of brain tumor or any striking growth in length such as is seen in those

tumors with which premature sex development comes relatively late; contrary to conditions as found in our patient. It may also be of interest to mention that Boehm found twelve cases of pineal tumor, all in *boys*. The sex glands in our case could not be felt, but we found a tumor in connection with and above the left kidney.

The hirsuties or virilism in question was therefore supposed to be due to a tumor of the suprarenal gland cortex. The question of operation now arose, but both Prof. P. Bull and Dr. Backer-Gröndahl considered the risk too great at so early an age and preferred to wait a year. We let the matter rest, as the child's good general health, as well as the slow growth of the tumor, pointed to its mildness. Thymus tablet treatment was instituted, and the child was sent home, Oct. 10, 1920.

I then wrote of the case to the head physician at Aalesund Hospital, Dr. Brekke, and, on the basis of our findings, and as on examination he also found a tumor, he determined to operate on the child.

Second Admission.—The patient entered the Aalesund Hospital, May 20, 1921. In the meantime, she had taken about 100 thymus tablets. In the opinion of the mother and others, there had been an improvement in the child's appearance since her stay in the State Hospital, especially after a severe throat attack with fever in December, 1920. The child could now walk and talk; she was not so fat, and some hairs on the face, and perhaps also on the mons pubis, had fallen out. The voice was just as deep.

A photograph, taken in April, 1921, seems to confirm this opinion. Dr. Brekke found the child certainly very large, but otherwise not striking, apart from her voice and the abnormal hair growth. She had as before sixteen teeth, and the tumor did not appear to have increased.

The day after admission to hospital, Dr. Brekke made an incision over the left groin and through it felt both ovaries, tubes and uterus, which all appeared normal. The left ovary, which was brought forward in the incision, looked normal, it being the size of a bean, oblong, whitish, hard and slightly indented in the middle.

Operation.—Five days later, the tumor was removed through an incision in the region of the kidney without bleeding. The patient was under ether for thirty-five minutes. The kidney was normal, with no connection with the tumor. The latter lay high up, and extended to the columna. The patient recovered quickly and was entirely well in a few days. The temperature rose to 102.6 F. (39.2 C.) the first evening but soon fell to normal. The tumor was sent to Professor Harbitz, in Christiania, who kindly placed at my disposal the result of his examination, including drawings of the microscopic dissections. "The specimen, a 3.5 by 2.5 by 2.2 cm. irregular curled tumor, weighing 10 gm., presented a surface covered with fibres of varying thickness. The consistency was somewhat variable, in part quite firm, in part soft. The surface of the cut had a lobed, complex appearance, divided into rounded compartments of different colors and appearance (Figs. 5 and 6). In several compartments, one could see a soft, homogeneous, red-brown growth tissue; in others, by the side of the first, a homogeneous yellow-gray center surrounded by a 2 or 3 mm. broad necrotic yellow-white area. In these compartments, lime was embedded. A number of smaller divisions, up to the size of a pea, had a yellow-white, almost cheeselike appearance.

"*Microscopic Examination* (Professor Harbitz).—The surface of the tumor was to a great extent covered with fibrous, partly hyaline degenerated tissue. Along the periphery, a brim of the original suprarenal substance was seen. Only a small part of the cells here were recognizable, as the suprarenal gland cortex

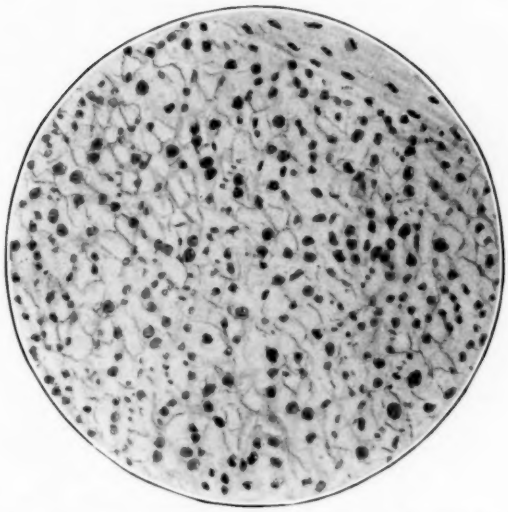

Fig. 5.—Cross-section of hypernephroma, showing regular structure.

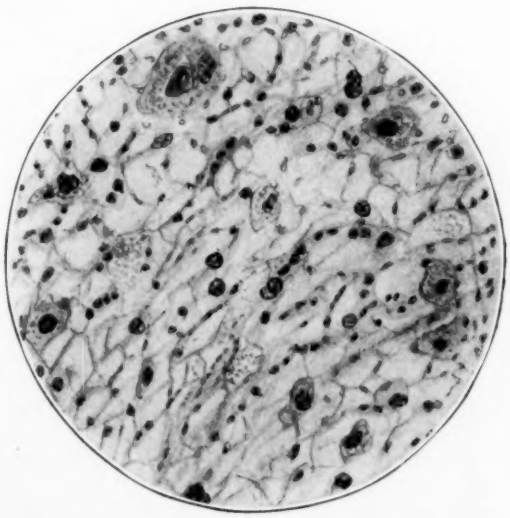

Fig. 6.—Cross-section of hypernephroma, showing irregular cell forms.

cells were arranged in clumps and strings. For the greater part, this tissue was infiltrated with cells resembling lymphocytes. There was also a diffuse fibrous area of neoplasia together with some bleeding in this tissue. The remains of the suprarenal glands above mentioned were found around large parts of the periphery of the tumor and in two diametrically opposite places. Besides the shell of suprarenal tissue above mentioned, which forms more obvious compact masses, there was also in this fibrous inlying capsule, in a long strip, small cell hoops of suprarenal epithelium, which gradually became unrecognizable. No extension into the distinct suprarenal gland marrow was seen. On the contrary, there were in the fibrous tissue in a few places clumps of a partly more compact and partly perforated tissue. Here also was found a markedly cellular and small-celled fibrous tissue, a part divided by fine meshes of fibrous tissue with large epithelium-like cells (Figs. 5). There was no sharp boundary between these two portions. The last mentioned parts showed cell forms of the type found in the large protuberances of which we shall speak later. The actual cellular, soft parts of the tumor were formed of a loosely built polymorphous-cell tissue. Among the cells, there was a small number of undifferentiated globular intercellular substances. The cells were of various kinds:

"1. There were numerous large spreading polymorphous giant cells and with one large nucleus or up to from eight to ten smaller nuclei. The protoplasm was bright-red (eosin). The large nucleus was rich in chromatin, and had, partly, a bladder-like appearance. In a specimen, sudan-stained, it was proved that the nuclei contained fat.

"2. By the side of the giant-cells were seen, as the most essential cells of the tumor, smaller, slightly polymorphous, well limited and distinctly epithelial cells with round nuclei. These cells partly resembled suprarenal cortex cells (Fig. 6).

"3. As a third type were found small spool-shaped fibrous tissue-like cells. These partly formed a net in the growth tissue, and partly appeared as a more distinct portion of the tumor.

"4. Spread out in the tumor tissue and somewhat unevenly divided were small lymphocyte-like cells. The form and size of the nuclei were somewhat variable.

"By the side of these there were found undoubted lymphocytes, partly in the growth tissue, partly in the adjacent granulating tissue.

"The yellowish white necrotic compartments and inlying lime particles appeared under the microscope only as a dull, degenerated structureless mass with lime sediment. The lime sediment was also found in the fibrous tissue on the outer part of the specimen. On the whole, these larger knots were built up of a scanty stroma, with the embedded large masses of cells probably of epithelial origin but rather polymorphous, especially in the oldest follicles. In the slightly degenerated, apparently younger follicles, the cell type had a distinct likeness to the suprarenal cortex. The tumor was confined by a thin shell of normal cortex which in some places, extending inward, was lost in the real growth tissue. The tumor itself consisted mostly of well-defined follicles filled with epithelial cells, which to a less degree resembled the suprarenal cortex (Fig. 5), but in the largest and the most numerous parts showed polymorphous large, multinuclear cell forms, even large giant cells (Fig. 6).

"However, there were found all intermediate forms in the epithelium mentioned. Judging by their formation, there was reason to consider these cells as chromaffin cells from the suprarenal marrow; but taking everything into consideration, it seemed most reasonable to consider the tumor as developing from the cortex, as a typical hypernephroma of rather long standing, as shown by degeneration and necrosis. On the whole, the tumor agreed in its structure fairly well with the suprarenal tumors found in similar cases described and illustrated by Glynn (1921).

"The structure, and not the least the small cast-off parts of the suprarenal cortex in the side of the tumor, suggested not a little a case of multiple tumor as

described by Harbitz,[17] a hypernephroma in a kidney, a chromaffin tumor in the region of the suprarenal gland, a similar tumor in the region of the kidney, together with, finally, a cystadenoma in the pancreas in a 47-year-old man, who however did not show any disturbances in his development."

Later Examination (July 27, 1922).—The child's appearance was strikingly improved, the face being far less bulging, without an abnormal growth of hair. The skin was smooth and fine, appearing more childlike. All abnormal hair growth had disappeared except scanty, short, dark hairs on the labia majora. The labia and mons pubis were less projecting than before. The peniculus was perhaps somewhat smaller. The whole body, especially the abdomen, was less fat, and the umbilical hernia was smaller. The voice was deep, with changes to treble as before, but not hoarse. The child ran about in a lively fashion, talked well and was intelligent. She was nervous and at times depressed.

May 4, 1923: The height was 109 cm.; weight, 20.5 kg. There was still some hair on the labia. The child was lively and intelligent. Her voice was as before.

COMMENT

The tumor—the cause of the masculating process—must in the present case have arisen in the later part of the fetal life, at a time when the sex organs are nearly but not quite formed (urethral furrow on peniculus) perhaps in the fifth or sixth month. As evidence of this fact, the tumor proved to be of relatively early origin, as it was infiltrated with lime (lime-atrophy). Whether the mother's nervous shock in the early months of pregnancy had a casual connection with the formation of the tumor cannot be determined. The patient presented the picture of a partial hermaphrodism (Lipschütz) or, if you will, a feminine pseudohermaphrodism, and presented, according to Apert's classification of hyperepinephry, the type for the fetal period, that form which Gallais calls "le pseudo-hermafrodisme surrénal." Apart from the urethral furrow, the case represented in all respects more nearly his "virilisme suprarenal," in which the injury occurs after birth. With regard to the course, the obvious stoppage in the development of the virilism, which occurred especially after a severe throat affection, and the improvement which her relatives apparently observed in the last months before the operation, are of interest. If such a stoppage or improvement really took place, it could be explained by the thymus therapy, which in my opinion is not very reasonable, or through the quite extensive hyaline degeneration and calcatrophy in the tumor, which may have entailed a decrease of the secretion of masculine hormones. This latter explanation might find support in the circumstance that the tumor does not appear to have grown from September, 1920, to May, 1921; that is, for eight months.

After the operation, I noticed an essential improvement in the patient's condition, so that the influence of the tumor was not doubtful.

17. Harbitz: Tumors in the Sympathic Nervous System and in the Suprarenal Medullary, Norsk Mag. f. Lægevidensk., No. 1, 1915.

While all signs of virilism have not yet disappeared, even after two years (May, 1923), the condition is all that could be reasonably expected as far as several symptoms are concerned.

The voice, for example, will scarcely become more childish, as the larynx cannot be supposed to have the plasticity necessary for it to decrease in size. The hypertrophy of the clitoris will probably decrease, but the urethral furrow will remain.

On the contrary, ossification will certainly by degrees come to correspond to the age, and the pelvis will probably attain normal dimensions.

The hair growth is easily influenced; therefore, as might be expected, the hirsutism almost vanished soon after the operation. However, there is still a scanty growth on the pubes. Perhaps this is unimportant, but one cannot overlook the fact that there may be a hyperplasia of the right suprarenal cortex. It must be noted that the right kidney is palpable, which is not usual at that age.

It may indeed also be thought that other endocrine organs enter into the question.

The prognosis for our patient attaining adult age is good, if the disposition to tumor does not lead to the development of tumors of a malignant type.

Judging from the literature, our patient is the first child with the genitosuprarenal syndrome who has survived removal of the tumor. So much the more interesting will it be therefore to follow her future. Hijman's 3-year-old patient, a girl, died from shock; Linser's, a 5-year-old boy, after an exploratory laparotomy. Schiff's [18] patient, a 2-year-old girl; Dobbertin's, a 14-months-old girl, and Adam's, a 14-year-old boy, died shortly after the operation. There is therefore every reason to congratulate Dr. Brekke on the good result of his operation.

Without the operation, in all probability the child would at an early age have developed into a short overly fat, bearded woman. Perhaps one cannot, however, with the quiescent period of the disease in mind, quite disregard the possibility that the tumor might have ceased to grow and entirely atrophied, and that there might have been a spontaneous return to health.[19]

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18. Schiff, Erwin: Frühzeitige Entwickelung der sekundären Geschlechtskarakteristiken bei einem zweijährigen Mädchen infolge eines Hypernephroms der rechten Nebenniere, Jahrb. f. Kinderh. **87**:519, 1918.

19. An extensive bibliography is found in Gallais (1914).

THE TEETH IN CHILDHOOD*

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The prevention of disease and the early recognition of physical and mental defects have long been the pride of pediatricians; the same should be true of the prevention of mental disease and the early recognition of dental defects. More and more parents are bringing their children to the physician with the request that routine physical examinations be made to see if the child is normal, and he then has an opportunity which may not be afforded the dentist until much later. Unfortunately, in the "complete" examination, the teeth are often overlooked. The responsibility for the prevention of dental disorders rests as much with the physician as with the dentist, and more especially with the pediatrician, who alone has ample opportunity to study the teeth of the child, and can often refer to the dentist children who might not otherwise be taken to him.

In the recognition of anomalous dentition, a familiarity with the time of eruption of the permanent teeth[1] is important. The curves in Figure 1, devised by Lyons and myself, represent the limits in the time and the average time of the eruption of the permanent teeth in 3,000 children between the ages of 5 and 13 years, observed in Rochester and in Olmsted County. The number of teeth erupted are charted in three-month periods. It will be seen that there is a marked irregularity in the time of eruption. For example, in one child, all four 6-year molars may have erupted by the age of 5 years; whereas, in another, they may not be in place until 7 years and 9 months, the average time of eruption being at the age of 6 years. Again, all twenty-eight permanent teeth may have erupted as early as 9 years and 9 months, or may not be in place even at the age of 13 years, 12 years being the average age for full eruption. In a larger series, there would, in all probability, be a few cases showing more premature eruption of the permanent teeth.[1]

Figure 2 shows the line given in dental textbooks to represent the time of eruption of the permanent teeth. The mean of the average time of eruption in our series indicates earlier eruption, probably because we have charted the time in three-month periods instead of one-year periods,

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* Received for publication, Nov. 26, 1923.

* From the Section on Pediatrics, Mayo Clinic.

1. James, W. W., and Pitts, A. T.: Some Notes on the Dates of Eruption in 4,850 Children, Aged Under 12, Proc. Roy. Soc. Med. **5**:80-101, Pt. 5, Sect. Odont., 1912.

or possibly because the permanent teeth are erupting earlier than formerly, as a result of dental caries and early loss of the deciduous teeth.

Not only is there a variation in the time of eruption, but there is also a marked variation in the order of appearance of the different permanent teeth.[1] The first permanent teeth are the 6-year molars, which come in distal to the temporary molars. These are rarely recognized as permanent by the parents and often not by physicians, and are, therefore, allowed to decay. It is the duty of every pediatrician

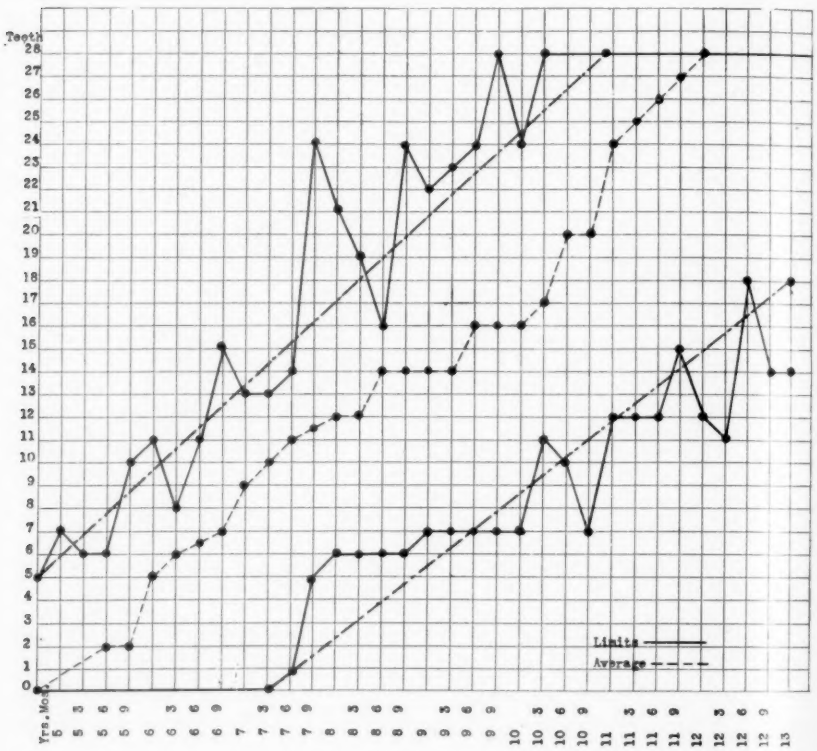

Fig. 1.—Erupted permanent teeth charted in three-month periods. The curves show normal limits and average time of eruption.

to point out these teeth to parents, so that measures may be taken for their preservation. The next teeth to appear are the lower central incisors, which are followed closely by the upper central incisors. Occasionally they appear coincident with, or prior to, the 6-year molars. The lower and then the upper lateral incisors are next in order. After the 6-year molars and the incisors are in, there is no more orderly eruption. Usually, there is a tendency for the corresponding mandib-

ular teeth to erupt prior to the maxillary ones. The first bicuspids usually erupt in order after the incisors. These are followed by the second biscuspids, and then by the canines or the second molars. The mandibular canines often erupt in order after the lateral incisors. The time of eruption of the permanent teeth seems to have a definite relation to the decay and premature extraction of the deciduous teeth.

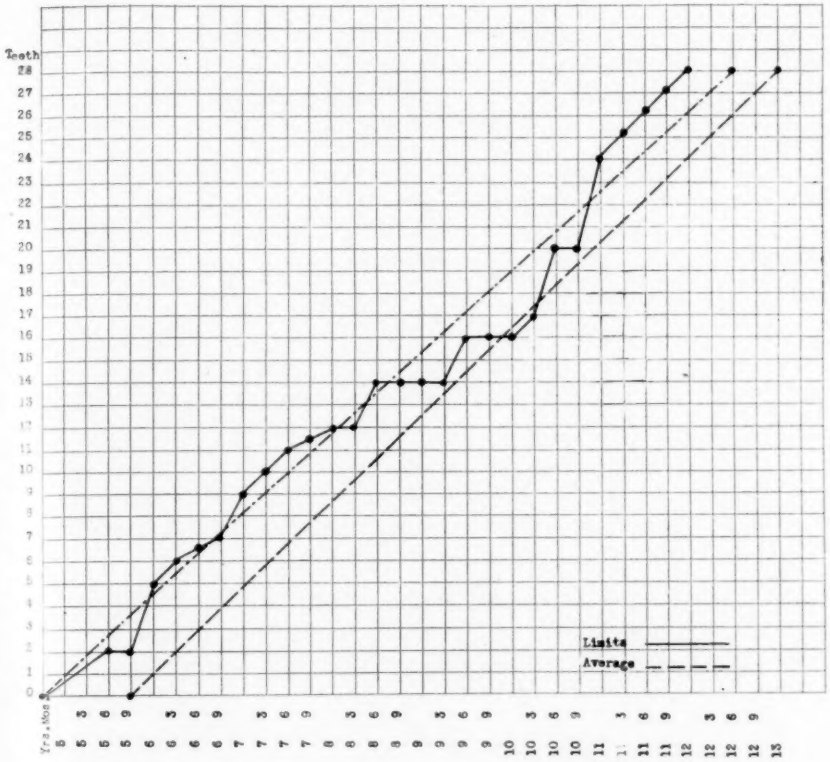

Fig. 2.—Erupted permanent teeth charted in three-month periods. The curve shows the average time of eruption. The upper dotted line represents the mean of this curve; the lower dotted line, the average time of eruption usually given in dental textbooks.

If the deciduous tooth is lost early, there is a tendency for the corresponding permanent tooth to erupt early.

The recognition of malocclusion early in childhood is of vital importance.[2] It is wise always to count the teeth and to notice whether the space is wide enough to allow each tooth to erupt. Between the ages

2. McCauley, C. M.: Preventive Orthodontia, Internat. J. Orthodontia **7**: 529-533, 1921.

of 4 and 4½ years, the temporary teeth should begin to show a certain amount of spacing, especially in the incisor group.[3]

There are two schools of orthodontia. The members of one school believe in the early treatment of any malocclusion which is present, or imminent.[4] If possible, they prefer seeing the child prior to the age of 4 years, when, by examination, they can detect early pathologic lesions, and by means of the roentgen ray see anything unusual in the unerupted permanent teeth.[5] Deformities of the maxillary denture due to thumb-sucking; those coincident with nasal stenosis from tonsils and adenoids, and those due to premature loss of deciduous teeth can be beneficially treated at this time.[6] If treatment of the deciduous or early permanent teeth is begun early, while the bones are pliable, simple devices are effective, and the periods of treatment short, although, of course, long observation is necessary to avoid recurrence.

Orthodontists of the other school believe in later treatment, after the bicuspid teeth are in place, which is usually after 10 years of age, when the parts are less pliable, and apparatus must needs be more cumbersome and be retained for months or years. It is strange how firmly the idea has become fixed in the minds of physicians and the laity that the time for orthodontia is at the age of 12 or 13 years. If put off until this time, it is usually postponed for life. It is clearly the duty of the physician to assist the orthodontist to map out this plan of treatment as early as possible; however, early interference with the temporary dentures is not advisable unless the condition has arisen from some local cause which nature will not correct.[6]

The common cause of malocclusion is the early loss of the deciduous teeth from decay, and this is largely preventable.[3] Inherited forms of malocclusion represent only an exceedingly small percentage of cases.[7] Ten per cent. of the 3,000 children observed were found to have serious malocclusion, and 50 per cent. had moderate malocclusion. According to Lyons, 65 per cent. of 267 children between 5 and 15 years of age passing through the dental department of the Mayo Clinic had malocclusion, 85 per cent. of which was due to the early extraction of deciduous teeth. When one realizes that not even 1 per cent. of the patients with severe

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3. Kregarman, S. L.: Prevention Versus Treatment of Malocclusion, Internat. J. Orthodontia **6**:222-229, 1920.

4. Bogue, E. A.: Early Treatment of Malocclusion, Internat. J. Orthodontia **8**:119-128, 1922.

5. James, W. W.: A Theory of Eruption, Internat. J. Orthodontia, **9**:676-683, 1923; McCauley: Footnote 2.

6. Case, C. S.: Etiologic Influences of Deciduous and Erupting Permanent Teeth, with Principles of Treatment, Internat. J. Orthodontia **7**:131-137, 1921.

7. Chapman, H.: Orthodontics: The Bearing of Etiology on Treatment, Internat. J. Orthodontia **9**:93-119, 1923.

malocclusion ever receive orthodontic treatment, the importance of prevention by preservation of the deciduous teeth until the time of their normal exfoliation is evident.

INHERITED DENTAL ABNORMALITIES

There are certain inherited dental abnormalities which it is important to recognize and which usually affect only the permanent dentition. Congenital absence of any permanent teeth may occur. Absence of one or both upper lateral incisors is the most common. Extraction of the tooth opposite the absent one, although not always necessary, is one of the few instances in which extraction is justified in the treatment of malocclusion.

Impaction also occurs commonly, most often in the bicuspid group, although any tooth may be impacted. It may occasionally be an inherited abnormality, but it is usually acquired, and is the result of crowding due to the too early loss of deciduous teeth. The 6-year molar may be impacted against the deciduous molar, but usually, if missing after 7 years of age, it has been prematurely extracted. The canine tooth is variable in its time of eruption and is prone to appear in an anomalous position. If there is space for it, it will tend to come into normal occlusion, but as this space is often compromised, it is commonly out of occlusion. Other inherited dental abnormalities are bifid bicuspids, pegged lateral incisors and short, broad upper incisors with long, narrow lower ones.

APLASIA

Various forms of aplasia occur in the permanent teeth. A number of children, both in the schools and in the Mayo Clinic, have been seen with the so-called collar and sleeve deformity. In this type of aplasia, the upper half of the crown is defectively enameled and is often a mere jagged stump. The mulberry molar is a manifestation of this condition in the 6-year molar. The 6-year molar and the incisors seem almost always to be involved when this deformity is present. In one case, the upper lateral incisors were not affected (Fig. 3). The first bicuspids and the canines have also often been affected. In this series, the second bicuspids and the second molars were not affected. A similar deformity in the deciduous teeth was observed in only one child, in whom all four canine teeth were involved, and the lower incisor teeth showed caries about the roots, only the roots of the upper incisors remaining intact (Fig. 4). Such aplasia was present in 0.5 per cent. of 3,000 children examined.

Defective enamelization in the form of multiple pitting was less common. The cause of this form of aplasia and of the collar and sleeve type is unknown. All of the children seen at the Mayo Clinic had negative Wassermann reactions, and none of the children seen in

school had any stigmas of hereditary syphilis. If the sleeve and collar deformity is seen in cases of hereditary syphilis, it must mean that it is a coincidence, or that a variety of causes have acted to produce the condition. It has also been attributed to exanthematous diseases, but in the case shown with involvement of the deciduous teeth, such could not have been the case; for the crowns of these teeth were fully formed prior to birth.[8] In other cases, we have been unable to get any history of contagious diseases. These children are usually healthy and normal in other respects. Although presumably some infection must be the causative factor, the specific infection, selective localization and comparative rarity of the condition is still unsolved.

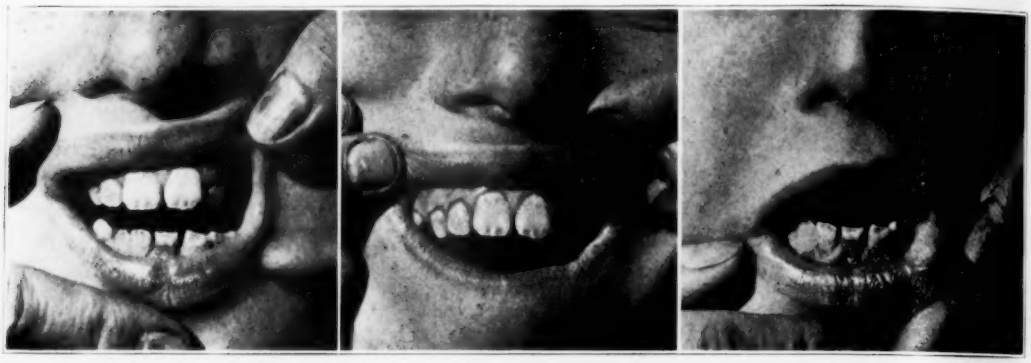

Fig. 3 (Patient, aged 12 years).—Appearance of front teeth. There were eighteen permanent teeth, with collar and sleeve deformity of 6 year molars, four lower incisors and two upper central incisors. The other teeth were normal. The patient had had measles, parotitis, diphtheria, pertussis and a discharging ear. The general health was good, the weight, normal. There were no signs of rickets, and the Wassermann reaction was negative.

FIFTH CUSP

Another phenomenon about which there is much confusion in the literature is the presence of the so-called fifth cusp. This is simply an atavistic remnant and is of no significance.[9] In a large series of cases, it was found to be present in 50 per cent., whether the child was normal or was suffering from divers ailments. The upper deciduous molars and the upper 6-year molars were the teeth presenting this cusp. It is occasionally unilateral; is rarely seen on any other tooth, and is extremely variable in size and appearance. Sometimes, it is merely a tiny projection on the surface of the teeth; again, it may be as large as any of the four other cusps of which the tooth is formed. Its

8. Blay, C. P.: The Care of the Teeth in Relation to Motherhood and Infancy, abstr. Internat. J. Orthodontia **6**:194, 1920.

9. Baudouin, M.: Anatomical Demonstration of Atavistic Origin of Fifth Cusp, abstr. Internat. J. Orthodontia **6**:331, 1920.

presence probably has no relation to the child's general health, or the condition of the teeth, although it has often seemed that such a tooth is unusually sturdy and strong. The absurd use of mixed treatment and other forms of antisyphilitic treatment on the theory that this is a syphilitic manifestation has no foundation.

SYPHILIS AS A FACTOR IN MALFORMATION

A study of the permanent upper central incisors has also been made. It was found that in 12 per cent. of children digitations were present, regular and of full height. In 48 per cent., the digitations were slight or absent, and the biting edge of the tooth was straight and even. In 40 per cent., the digitations were irregular or the biting edge was irregular and uneven (Fig. 5). It is this last group of 40 per cent. which is so

Fig. 4 (Patient, aged 2½ years).—Appearance of front teeth. There were twenty deciduous teeth. The four canines only showed collar and sleeve deformity. The upper right and lower left molars and all lower incisors showed deficient enamel on the anterior surface. Only the roots of the upper incisors remained. The patient had pneumonia at the age of 1 year. There was marked prominence of the occiput. The child was 16 per cent. underweight. The Wassermann reaction was negative.

often wrongly spoken of as suggestive Hutchinson's teeth. Furthermore, 12 per cent. were found to have convergent sides which might simulate the so-called chisel-shaped teeth of hereditary syphilis. The anteroposterior thickening, so common in the typical permanent upper central incisor of hereditary syphilis, was rarely seen in nonsyphilitic patients. From these observations and the observation of the teeth in many cases of hereditary syphilis, it would appear that the concavity on the biting edge, the anteroposterior thickening and the convergent

and often convex sides, all taken together, and applying only to the upper permanent incisors, are the only dental signs which are pathognomonic of hereditary syphilis. If there is the shadow of a doubt about the teeth being Hutchinson's, they are usually not. The deciduous teeth are never pathognomonic, and no authentic case of Hutchinson's teeth in the deciduous incisors has ever been reported. The pegged or chisel-shaped permanent upper lateral incisors are an inherited abnormality and not pathognomonic of hereditary syphilis. Stokes and Gardner report a case of hereditary syphilis in which Hutchinson's teeth were diagnosed by roentgen ray prior to their eruption.[10] Such a diagnosis is only applicable after the permanent crowns

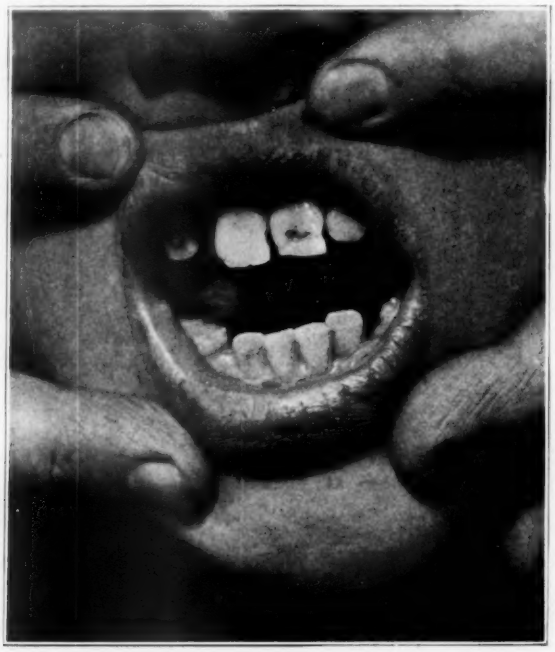

Fig. 5 (Patient, aged 10½ years).—Appearance of front teeth. There were fourteen permanent teeth. The anterior surfaces of the permanent upper central incisors were irregular and discolored. The lower one fourth of the crown was thin, and narrower than the upper three fourths. The digitations were irregular on the right and absent on the left. The patient had had measles only. A marked funnel chest and scaphoid scapulae were noted. The patient was 16 per cent. underweight. The Wassermann reaction was negative.

are fully formed. It is, therefore, valuable confirmatory evidence in cases of suspected syphilis prior to the eruption of these teeth. However, in only a small percentage of cases of hereditary syphilis are

10. Stokes, J. H., and Gardner, B. S.: Demonstration of Unerupted Hutchinson's Teeth by the Roentgen Ray, J. A. M. A. **80**:28-29 (Jan. 6) 1923.

Hutchinson's teeth present, so that other more constant signs, a suggestive history and a laboratory investigation are more valuable in the diagnosis.

DENTAL CARIES

The question of dental caries is most vital to the physician and to the patient. As is well-known, caries is most prevalent in infancy, childhood and adolescence, and it is in these periods that prevention must be practiced.[11] In infancy, this consists mainly in the prevention of malnutrition and underfeeding in elements necessary for building dental structure.[12] Frequent and systematic observation and cleansing of the teeth from the time of their eruption are essential, and cleansing of the teeth by proper food at the end of each meal is preferable to the use of the tooth brush.[13] Thumb sucking, with its resultant malocclusion, should, of course, be guarded against. If it has caused irregularity of the maxillary denture, daily pressure should be employed to correct this deformity. Although breast-feeding is, of course, the ideal feeding, it is not essential in the prevention of either caries or malocclusion. If infants are properly fed artificially and normal nutrition is maintained, normal development of the teeth and jaws will result. The control of the nutrition and diet of the mother during pregnancy is important.[8] If lancing of the gums in infancy should become necessary, it should be done by the dentist with the actual cautery.[14]

In childhood and adolescence, prevention of caries is largely dependent on the cleansing of the teeth and on the prevention of general infections. It is well known that the teeth often decay rapidly during and after febrile diseases. Much of this is due to the fact that during illness the teeth are not so likely to be kept clean, and that elevation of temperature causes any residual food on the teeth to decay more quickly and form a nucleus for beginning caries.[11] Conversely, it must be remembered that prevention of caries by the elimination of the teeth as foci may reduce the incidence of communicable disease.[15] Of course, the diet is as important during childhood and adolescence as during infancy, for the permanent teeth are being formed at the same time as the temporary ones are being maintained.[16]

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11. Millberry, G. S.: The Problem of Dental Hygiene in Children, Arch. Pediat. **33**:533-538 (July) 1916.

12. Talbot, F. B.: The Relation of Diet to the Development of Children with Special Reference to the Teeth, M. Clin. N. America **2**:1333-1340 (March) 1919.

13. Gibbs, J. H.: Child Welfare and the Prevention of Dental Disease, Edinburgh M. J. **18**:433-441 (June) 1917.

14. Barker, P. A.: Operative Procedure on Children's Teeth, J. A. D. A. **10**:527-534, 1923.

15. Clark, T., and Butler, H. B.: Children's Teeth, a Community Responsibility, Pub. Health Rep. **35**:2763-2779 (Nov. 19) 1920.

16. Mellanby: The Value of the Animal Experimental Method in Dental Research, Dental Rec. **42**:1-12, 1922.

How can the physician help to eliminate the occurrence of dental caries? The goal we seek is that no deciduous tooth be extracted until the corresponding permanent tooth is ready to take its place. This is normally at the time when the arch is large enough to support the permanent tooth in normal occlusion. Evidently, then, cavities should be filled when they are small.[14] However, it must be borne in mind that any deciduous tooth which is not devitalized can and should be filled. If the roots of deciduous teeth have not yet begun to be absorbed, even the root canals may be nicely filled.[17] In general, however, all devitalized teeth should be removed immediately, as they are a source of peril to the very life of the patient, and the maintenance of the normal arch becomes of secondary importance.[18] The pulps of deciduous teeth are larger in proportion to the size of the teeth than are those of the permanent teeth. Also the wall of dentin is thinner, so that slight decay is dangerous.[17] Therefore, a roentgen-ray examination of carious teeth is often necessary, if the proper treatment is to be instituted.

As regards the treatment of radial caries, the proximal decay can be cut away,[17] or the decay may be arrested by the application of strong silver nitrate solution.[19] The latter treatment is preferred by most dentists. I have seen teeth that were affected by radial caries beautifully filled by clever dentists.

Broken off incisors are common in childhood. If deciduous teeth are broken, decay should be arrested, if possible, and the teeth kept in place until time for the permanent teeth to erupt. Decay, if it occurs in the permanent teeth, should also be arrested. If the pulp is uninjured, the teeth can be built up after they have grown to be large enough so that lateral pegging can be done without injury to the pulp cavity. This can usually be accomplished about four or five years after the time of eruption of the tooth, or at the approach of puberty. If the pulp is injured, the broken-off, permanent teeth will have to be removed and replaced by artificial teeth at the time of puberty. It is important to remember that teeth can become devitalized by trauma which is not sufficient to break off any part of the crown. These teeth may or may not become black. The trauma may, and probably will, cause a root injury.

The importance of the sixth year molars should be emphasized. They are the keystones of normal occlusion in the mouth, and as such their preservation is essential.[3] When they first come in, they often have deep incisuras, which retain food easily. Early decay along these

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17. Black, G. V.: A Work on Special Dental Pathology, Chicago, Medico-Dental Publishing Co., 1915, 489 pp.

18. Perry, R. H.: The Medical Aspect of Dental Caries in Childhood, J. Tennessee M. A. **11**:257-264 (Nov.) 1918.

19. Beischer, A. L.: Treatment of Deciduous Teeth, abstr. Internat. J. Orthodontia **7**:458, 1921.

deep crevices in the crown is common. Prophylactic soft fillings can be placed in these crowns to advantage, even though decay has not begun.[17] When the teeth are full-sized and completely erupted, these fillings may be removed or allowed to wear themselves out. In this way, the permanent tooth, which is most subject to decay, will be saved, and the time of most prevalent decay will be safely passed.

SUMMARY

The pediatrician, because of his unique opportunity for early observation, should share responsibility with the dentist in preventing malocclusion, decay and infection in the teeth of children. If the physician will inform himself with regard to the normal and abnormal development of teeth, and in every routine examination of a child will observe the condition of its teeth and emphasize the importance of their proper care, much disease and decay will be avoided.

TWO CASES OF ACUTE EPIDEMIC ENCEPHALITIS OCCURRING IN ONE FAMILY*

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Since the beginning of the epidemic of acute encephalitis, many articles have been written regarding the question of contagion in this protean disease. Netter,[1] Stern,[2] Flexner,[3] Stiefler,[4] Wechsler,[5] Guillian and Lechelle,[6] de Laroche,[7] Lévy,[8] Fyfe,[9] Lemierre[10] and, recently, Hunt,[11] in a report of the 1923 New York epidemic, have contributed case reports to the literature or have summarized a large number of cases in which the element of contagion is freely discussed. This question is a very important one in the hospital management of the disease. The object of this paper is to report two cases of acute epidemic encephalitis occurring in one family. The fact that both of these cases developed under very poor hygienic conditions in which a family of five were living in the same room must be considered. All five members of the family were affected with an influenzal condition approximately at the same time.

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* Received for publication, Dec. 7, 1923.
* From the Neuropsychiatric Clinic, Philadelphia General Hospital.
* Read before the Philadelphia Neurological Society, Nov. 23, 1923.

1. Netter, A.: Contagiousness of Lethargic Encephalitis, Bull. Acad. de méd. **83**:373 (April 27) 1920.

2. Stern, Felix: Die Epidemische Encephalitis, Berlin, Julius Springer, 1922.

3. Flexner, Simon: Lethargic Encephalitis, Pathologic and Clinical Features and Epidermiology in Brief, J. A. M. A. **74**:865 (March 27) 1920.

4. Stiefler, George: Contagiousness of Epidemic Encephalitis, Ztschr. f. d. ges. Neurol. u. Psychiat. **74**:396, 1922; abstr. December, 1922, p. 694.

5. Wechsler, I. S.: Statistics of Epidemic Encephalitis, Neurol. Bull. **3**:87 (March) 1921.

6. Guillian, G., and Lechelle, P.: A Case of Contagion in Lethargic Encephalitis, Bull. Acad. de méd. **84**:321 (Dec. 14) 1920.

7. De Laroche: A Case of Familial Contagion in Lethargic Encephalitic, Paris méd. **10**:364 (Nov. 13) 1920.

8. Lévy, P. P.: Three Cases of Epidemic Encephalitis in One Family, Bull. et. mém. Soc. méd. d. hôp. de Paris **44**:1007 (July 9) 1920.

9. Fyfe, L. L.: Encephalitis Lethargica; An Intensive Outbreak in a Small School, Lancet **2**:379-381 (Feb. 24) 1923.

10. Lemierre, A.: Familial Epidemic Encephalitis; Probable Transmission of the Virus by a Person Affected for Three Years, Bull. et. mém. Soc. méd. d. hôp. de Paris **44**:1628 (Dec. 31) 1920.

11. Hunt, E. L.: Epidemic (Lethargic) Encephalitis: the Recent New York Epidemic, J. A. M. A. **81**:1352 (Oct. 20) 1923.

REPORT OF CASES

CASE 1.—M. M., girl, aged 13 years, in whom the onset of the present attack occurred in November, 1919, presented symptoms of a respiratory infection, with marked asthenia, many aches and pains and occasional vomiting. She was said to have had a cold in her head, also to have had a slight fever. On the second day, her mother noticed that her eyes were crossed, and she complained of double vision. For the next week, she showed typical findings of acute delirium, being very apprehensive and also having extensive visual hallucinations. She was in bed during this period of approximately two weeks. She was never lethargic, but suffered from marked insomnia with agitation at night. On getting up two weeks after the onset of illness, the patient developed choreiform movements, for which she had been treated for the past few years in various dispensaries. On the advice of a physician, she later had a tonsillectomy performed. In 1920, when she first reported to our neuropsychiatric clinic, routine physical examination revealed findings of a mitral stenosis. At this time, she showed typical generalized choreiform movements and was quite agitated. She was sent for a rest period in the country, where she remained for several months, until the choreiform movements disappeared. Neurologic examination revealed weakness of left external rectus, a unilateral ptosis, marked incoordination in finger to nose test, etc. On several occasions, she showed slight nystagmoid movements of the eyeballs. She frequently complained of diplopia. Otherwise, all examinations were negative. During the past year, she had shown no choreiform movements.

Secondary sex characteristics since puberty had been marked. She had been growing obese, but had not shown any behavior abnormalities in school, where her progress was normal. At home, she was very irritable, fussy, obstinate, sullen and quarrelsome, and showed a general emotional lability. No definite delinquent acts had been noted and behavior abnormalities for the most part had played an insignificant part as a sequel of the disease. During her last visit to the clinic, she had shown no evidence of incoordination of any description and apparently had been adjusting herself well to her surroundings.

Spinal fluid and blood examination, when she was admitted to the hospital, were all reported negative. Otherwise, the general examination was negative throughout.

CASE 2.—E. M., girl, aged 11 years, slept with M. M., and developed practically identical symptoms a few days later, her main complaints being headache and dizziness. Her eyes crossed more than M. M.'s, according to her mother's report. She had diplopia and had had a persistent strabismus ever since. For brief periods, she was delirious at night, reacting on several occasions to visual hallucinations. She had no radiculitis at this time, and no choreiform movements, and there have been no sequelae of neuropsychiatric significance in this case. She had been getting along very well in school, progressing normally for her age. Her mother stated that frequently she complained of pains through her arms and legs for a year following this illness, but these had ceased entirely and she had no subjective complaints at the present time. There were no neurologic sequelae, except a left internal strabismus, which appeared to be constant. A heart specialist stated that there was no damage to the valves. Laboratory examinations were all negative.

It may be wise to review the mother's attack at this time. She is said to have had a very severe attack of influenza, with the findings of acute respiratory infection and delirium. Her main complaints were headache, dizziness and visual impairment. Since she recovered from this illness, she felt there had been a gradual change in her vision. The eye grounds are negative at present. There was no history of insomnia or lethargy. She had complained of occasional pains in her arms since this illness.

COMMENT

Many interesting facts are suggested in the study of the two cases. First, the family group is interesting, and a diagnosis of a post-encephalitic condition in the two children appears most probable. There is some question about the mother having a similar illness. The fact that this developed following influenza is of interest in that we frequently have seen this relationship in other cases of encephalitis in children that we have studied. The statements in the literature seem to show that encephalitis frequently develops after influenzal conditions when the patient's resistance is lowered and he is most susceptible to a secondary invader such as may be present in the etiologic agent of acute epidemic encephalitis. Cases of this type suggest the latter possibility and confirm the reports of others in this regard. These two cases were the only ones seen by us in which encephalitis has occurred in two members of the family, in a large number of postencephalitic disturbances observed in both the outpatient clinic and the neuropsychiatric wards. The question regarding the transmittability of the virus causing encephalitis must be considered in the foregoing cases. Whether or not hospital isolation is essential will depend on further data. We do not practice isolation in our general hospital. No cases of hospital contagion have been reported in the literature, with the exception of those of Wechsler,[5] in which two interns in a hospital developed encephalitis. The rarity of instances of this type may well be looked on, therefore, as accidental. We feel that direct transmission in cases of encephalitis is almost negligible. Wechsler,[5] out of 864 cases found only five cases of the disease occurring in two members of the same family. This constitutes one half of 1 per cent. of the cases in which he has completed careful clinical statistical studies.

SUMMARY

In two cases of acute epidemic encephalitis in children of one family, the question of contagion and their relation to post-influenzal conditions were points of interest. The rarity of these instances suggests that they had better be looked on as accidental and that the factor of direct transmission in acute epidemic encephalitis, with the facts we have now at hand, is practically negligible.

KIDNEY DISEASES IN INFANTS AND CHILDREN

II. MALIGNANT HYPERTENSION NEPHRITIS: PRIMARY SCLEROTIC KIDNEY (SCHRUMPFNIERE) *

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In a previous paper,[1] we divided the cases of kidney disease seen by us into four groups, stating that the classification was based solely on (*a*) the clinical picture, (*b*) the duration of the disease and (*c*) the prognosis. We described the group called nephrosis, and now proceed to define another, which may be termed malignant hypertension nephritis in children. This group, of which we append three examples, is not very common in infancy and childhood, yet the picture is so clear cut that an absolute diagnosis and prognosis can be made.

REPORT OF CASES

CASE 1.—*History.*—S. G., a boy, aged 3½ years, of Russian parentage, was an only child. The father and mother both had positive Wassermann reactions, but, from the history of the father and the result of examination in the child, it seemed definitely established that the parental infection occurred long after the birth of the child.

The patient was supposed to have had measles, parotitis, diphtheria and scarlet fever. It was impossible to obtain the dates of these infections, and the accuracy of the information is not assured. Tonsillectomy had been performed a year previously.

Within the past four months, the child had complained of sharp pain in the epigastrium and right upper quadrant of the abdomen, occurring about one-half hour after meals. The pain had increased in severity and constancy, so that now it was present practically all the time. He vomited occasionally, but this did not relieve the pain. The vomitus did not contain blood. Constipation was marked. The child had had a voracious appetite and marked thirst for the past four months. During this time, he had nocturnal enuresis and passed large quantities of urine. He complained now of headache and felt weak and sick. He had had no dyspnea nor edema.

Examination.—The head was somewhat large and out of proportion to the body. The child appeared old and wrinkled, and the temporal arteries were plainly visible. The pupils reacted to light and in accommodation. The skin was brownish and very dry. The teeth were in fairly good shape. The tonsils had been enucleated. The pharynx was normal. The lungs were negative to auscultation and percussion. The heart's action was forcible. There was a faint systolic murmur, and a markedly accentuated second sound at the apex. The pulses wherever palpable were like pipe-stems—hard and noncompressible. The abdomen was soft and negative to percussion and palpation. The spleen was just palpable, and the liver was felt two fingers below the border of the ribs.

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* From the pediatric department of Mount Sinai Hospital.

1. Schwarz, Herman, and Kohn, J. L.: Nephritis in Children, Am. J. Dis. Child. **24**:125 (Aug.) 1922.

Blood pressure on admission was 250 systolic and 195 diastolic, and the Wassermann reaction of blood and spinal fluid was negative.

The blood examination showed erythrocytes, 5,200,000; leukocytes, 8,200; polymorphonuclear cells, 80 per cent.; and hemoglobin, 55 per cent. The phenolsulphonephthalein excretion was 56 per cent. in two hours.

Blood chemistry: The urea nitrogen was 16.8 mg. per hundred cubic centimeters of blood; incoagulable nitrogen, 50.3 mg.; uric acid nitrogen, 1.7 mg., and creatinin nitrogen, 1.3 mg. per hundred cubic centimeters of blood.

Urinalysis: A twenty-four hour specimen showed the volume to be 1,200 c.c. (with an intake of 800 c.c. of fluid); reaction, acid; specific gravity, 1,004, and a heavy trace of albumin. Microscopically, there were a few red and white blood cells.

Ophthalmologic examination (Dr. Julius Wolff): The nerve heads were red, and the margins obliterated and merged into the retina. An edema of one diopter was present. The arteries were narrow, fine, corkscrew vessels. There were fresh and old hemorrhages, and several spots of degeneration, especially in the region of the macula and the temporal side of the nerve head.

From the physical examination and the laboratory findings, we may deduce that the patient had markedly increased systolic and diastolic blood pressure, thickened arteries and moderate secondary anemia; no retention of nitrogenous products in the blood, a polyuria, and a urine of low specific gravity, with a moderate amount of albumin. The eyegrounds showed a typical neuroretinitis albuminurica.

TABLE 1.—*Fluid Intake and Urine Volume (c.c.)*

	Date											
	March				April						May	
	21	23	25	27	1	5	10	15	20	25	5	20
Intake....	550	950	855	1,520	750	800	1,200	1,100	1,400	800	1,100	200
Excretion	980	625	1,200	1,150	1,000	800	1,000	2,225	2,250	500	700	200

Patient moribund.

Course in Hospital.—The patient had been in the hospital two months when he died, so the entire course of his illness was about six months. During these two months in the hospital, the abdominal pain was constant and very severe. Benzyl benzoate, nitroglycerin and amyl nitrate were given without effect. During the last two weeks of the disease, the abdominal pain was even more marked, and there were large amounts of clotted blood in the stool. Roentgen-ray examination of the peripheral and abdominal arteries revealed no signs of calcification. The systolic blood pressure remained persistently high (around 200) during the entire time. The nitrogen determination of the blood serum repeated at three different periods showed no higher figures than at the first examination. The fluid intake and the urine volume can best be seen from the data presented in Table 1.

The specific gravity of the urine was always low, and microscopically a few hyaline and granular casts were occasionally seen. Death was due to inanition and hemorrhage. Necropsy was not permitted.

CASE 2.—*History.*—K. L., a girl, aged 11½ years, whose parents and a brother and sister were well, gave no history of kidney disease in the family, nor personal history of any infectious disease, except measles and pertussis eight years before. The patient was in excellent health and had a good appetite until the onset of this illness.

For the past six months, the child had not been looking so well, but there were no definite symptoms of any kind until six weeks previously, when the patient had begun to vimit and to have abdominal pain. The pain was cramp-like in character, and was located in the region of the umbilicus. The vomiting and pain continued every day, and often were present several times a day. In

addition, the child had a marked polyuria, voiding often every fifteen minutes, and many times at night. There were no headaches, no disturbances of vision, and no cardiac nor other symptoms.

Examination.—The patient was fairly well developed and well nourished, and did not appear acutely ill. The nose and throat were in good condition, and the skin was normal. The lungs were normal to percussion and auscultation. There was visible and palpable episternal pulsation of the heart. The apex beat was seen and felt in the sixth interspace, 8.5 cm. from the midsternal line. A definite, soft systolic murmur was heard at the apex, which was not transmitted. Palpation and percussion of the abdomen were negative. The spleen and liver were not palpable. The extremities showed no edema.

On admission, the erythrocytes numbered 4,480,000; leukocytes, 13,000, with polymorphonuclear cells, 87 per cent., and the hemoglobin, 78 per cent.

Blood chemistry: The urea nitrogen was 36.0 mg. per hundred cubic centimeters of blood; incoagulable nitrogen, 70.0 mg.; uric acid nitrogen, 3.0 mg.; creatinin nitrogen, 2.2 mg. per hundred cubic centimeters of blood; cholesterin, 0.320 per cent., and sugar, 0.075 per cent.

Urinalysis: The reaction was acid; specific gravity, 1.016; albumin, a heavy trace, and no sugar. Microscopically, a few hyaline and granular casts, and an occasional red blood cell were seen.

Ophthalmologic examination (Dr. Wolff): The left disk was white and was raised by a dense exudate containing small, shiny white spots. This exudate tapered off gradually for a considerable distance into the retina, and at its uppermost edge broke off into clusters of small, round exudate. The center of the disk was elevated from three to four diopters. The retinal veins were full and tortuous, but no hemorrhages were present. The right disk showed the same condition, but in a less degree. The systolic blood pressure was 205.

Roentgen-ray measurements of the heart were as follows: left transverse diameter, 7.75 cm.; right transverse diameter, 2.5 cm.; oblique diameter, 10.5 cm.; arch, 4.5 cm. Roentgen-ray examination of the various arteries was negative.

From the physical examination and the laboratory findings, we may deduce marked hypertension, some cardiac hypertrophy, polyuria, albuminuric retinitis and retention of nitrogenous substances in the blood.

Course in Hospital.—The patient's entire stay in the hospital was thirteen days. The duration of the acute symptoms was about eight weeks, and the entire course of the disease perhaps not more than eight months. The general condition became gradually worse; the abdominal pain was almost continuous, and the stools contained fresh and old clotted blood. The blood pressure remained high—from 180 to 240 systolic, and from 130 to 180 diastolic. The phenolsulphonephthalein excretion was 30 per cent. in two hours. The character of the urine remained the same, and the output was regularly as great, if not greater, than the absolute fluid intake.

Purpuric spots appeared all over the child's body during the last week of her illness, yet the blood platelet count was 200,000. She became drowsy and appeared suburemic during the last few days of her life. A chemical examination of the blood taken a few days before death showed a urea nitrogren of 85.4 mg. per hundred cubic centimeters of blood; incoagulable nitrogen, 146.5 mg.; uric acid nitrogen, 6.9 mg., and creatinin nitrogen, 2.8 mg. per hundred cubic centimeters of blood.

Necropsy Findings.—The body was that of a markedly emaciated child of normal size. There was no postmortem discoloration, no icterus and no rigor mortis.

Heart: The weight was 240 gm. The left ventricle was enormous, and was hypertrophied. The anterior aspect of the pericardium showed a small milk spot. The heart muscle on section was normal in appearance. The tricuspids and pulmonary orifices were normal. The mitral orifice showed a slight, uniform thickening of both cusps, probably of an arteriosclerotic nature. The aortic cusp along its aortic aspect presented three dry, yellow patches of atheroma;

the posterior wall of the outflow track showed the distinct whitening of endocarditis. The aortic cusps showed a marked arteriosclerotic thickening of the corpora arantii. The arch of the aorta was of normal width and elasticity. At the root, just above the sinus of Valsalva, were a few small yellowish atheromatous markings in the intima, beginning in the descending part of the arch and extending throughout the thoracic and abdominal aorta. The iliac vessels showed numerous button-like thickenings of the media, over which the intima appeared to be normal. On section, the centers of these thickenings were usually found to contain some yellow atheromatous material. These nodules in the thoracic aorta surrounded the orifice of the intercostal vessels and markedly narrowed them. The largest nodes were about the size of a thumb nail. The systemic vessels throughout the body appeared to be uniformly thickened.

Lungs: Both lungs on section were found to be edematous, and scattered through both lower lobes were small areas of diffuse hemorrhages. The weight of the left lung was 180 gm.; of the right lung, 220 gm.

Thymus: This was normal.

Liver: This was larger than normal, weighing 875 gm. The surface was bluish brown, and there was intense passive congestion.

Gall-bladder and bile passages: These were normal.

Spleen: The weight was 70 gm., and it was normal in size. On section, the malphighian bodies were seen to be extremely prominent, and the pulp was dark red and apparently congested.

Kidneys: The right kidney was about the size of a large lima bean, and weighed 6 gm. The capsule was adherent to the organ. On section, the cortex appeared to be 1 mm. in width. Striation could not be made out. The organ cut firmly. The pelvis was reduced in size in proportion to the size of the kidney. The ureter was of normal width. The left kidney weighed about 150 gm. and was slightly larger than normal. The capsule stripped easily, leaving a smooth surface, dirty yellowish brown, with diffuse, darkened mottling and occasional pin-point hemorrhages. On section, the cortex was yellowish brown, with streaks of lighter yellow, apparently fatty. The cortical parenchyma was swollen so that the striations were obscured. The medulla was intensely congested. The pelvis and ureters were normal.

Bladder and pancreas: These were apparently normal.

The suprarenals: These were normal in size. On section, the cortex was found to be thinner than normal. It appeared as a thin, dry yellow line. The greater part of both suprarenals appeared to consist of a markedly hyperplastic medulla.

Gastro-intestinal tract: The stomach showed a few scattered hemorrhages. On the posterior wall, near the lesser curvature, were two shallow ulcers about 1 cm. in width. The intestines were moderately dilated. About 18 inches of the ileum, 12 inches from the ileocecal valve, was gangrenous and bound down into the pelvis by adhesions. The omentum was adherent to the mass of gangrenous intestine. There appeared to be no volvulus. The arteries and veins leading to the gangrenous area were apparently normal. The process was therefore due to an intussusception which was spontaneously reduced before death.

Diagnosis: Congenital hypoplasia of the right kidney was diagnosed, with subacute nephritis of the left kidney, presenile arteriosclerosis, cardiac hypertrophy, acute intussusception and gangrene of the ileum.

Microscopic Examination.—The left kidney showed typical glomerulotubular nephritis, which was fairly diffuse in extent. The process was subacute. Some of the glomeruli showed necrosis of some loops. In all the glomeruli was a swelling of the endothelium, an increase in nuclei and an almost complete obliteration of the outlines of the capillaries. Here and there, some of the glomeruli and other contiguous tubules were well preserved. The arteries and arterioles in the cortex showed marked thickening of their walls. The larger

arteries were apparently not involved. In addition, there were areas in which the tubules were atrophic, and there was a marked increase in the interstitial connective tissue resembling replacement fibrosis. It is possible that some of these areas were examples of focal nephrosclerosis complicating diffuse nephritis. The right kidney showed a cortex—or what was left of it—consisting of a small amount of dense, purulent connective tissue in which were imbedded numerous glomeruli and strands of atrophic tubules. Only a few small islands of well preserved tubules were seen. The medullary portion of the section and also some of the cortical portion consisted of a dense connective tissue in which were imbedded atrophic tubules. There were numerous thick-walled arteries and arterioles, the latter showing an enormous hyaline thickening, especially of the intima, which markedly narrowed the lumen.

Spleen: There was marked hyaline thickening of the wall of the arteries and arterioles, and lymphoid hypoplasia.

Suprarenal: There was a marked increase in the medulla tissue. The section contained numerous thick-walled arteries.

Heart muscle: There was moderate hyaline thickening of both media and intima in many of the small arteries in the interstitial apaces.

Aorta: There was button-like thickening of the intima involving the adjacent portion of the media, consisting of a peculiar homogeneous matrix which stained greenish blue, looking almost like the matrix of myxomatous tissue. Scattered in it were spindle-shaped and star-shaped fibroblasts similar to those in myxomatous tissue. The media also showed streaks of degeneration scattered through it which took the same blue stain. This bluish material appeared to result from a peculiar degeneration of the entire elastic system in the media.

Arteries: The external iliac artery showed the same degeneration of the media as was seen in the aorta. The muscle fibers in the media were in places atrophic and were spread apart by a peculiar homogeneous bluish stain, apparently a degenerated part of the elastic substance. On one side of the vessel was a button-like thickening of the media, which consisted of the same myxomatous-like structure seen in the aorta. The lumen o fthe vessel was partially occluded by a mass of round cells and polymorphonuclear leukocytes imbedded in some fibers. The adventitia showed no changes that could be considered characteristic of syphilis. The common iliac arteries showed areas of degeneration in the media resembling those already described, but here they were more diffuse and more uniformly distributed within the circumference of the vessel.

Case 3.—A girl, aged 11½ years, whose mother, father, and five brothers and sisters were well, and who gave no history of familial disease of any sort, was a full-term child, of fair general health with poor appetite; always thin, and constipated. She had had pneumonia when 2 years of age, and was sick for ten weeks when 4 years old, the diagnosis being unknown. There had been no scarlet fever, diphtheria or pertussis. She had had nocturia during the past six months. There had been no epistaxis, fever or night sweats. The patient had had marked anemia for the last six or eight months.

The first symptoms of the present illness noted by the mother were swelling about the eyes and severe headaches. A urinalysis had been made for the first time about six weeks before admission to the hospital and had shown "kidney trouble." Four weeks before, the child had had a sudden attack of convulsions and coma lasting a few days, and another attack two weeks before. Slight edema of the legs had appeared a week previously. Anorexia was marked. Dyspnea, weakness and pallor were increasing.

Examination.—The child had a convulsion on admission to the hospital; her mind was dissociated, and she was in a semicomatose condition. Vision was so poor that she could scarcely recognize fingers at a distance. Nutrition was excellent. The skin was very pale, with slight puffiness about the face. The pupils reacted to light, and no abnormal reflexes were present. Teeth, tonsils

and pharynx were in good condition. The lungs were normal on percussion and auscultation. The heart was enlarged to the left. The apex beat was in the sixth interspace. The second sound at the base and at the apex was accentuated, and there were no murmurs. The radial arteries were not felt, and the temporal arteries were not visible. The pulse was rapid and of high tension. The abdomen was normal to palpation and percussion. The liver and spleen were not palpable. The extremities showed slight pretibial edema.

Blood examination: The erythrocytes numbered 1,660,000; leukocytes, 25,000, with polymorphonuclear cells, 87 per cent., and hemoglobin, 19 per cent.

Blood chemistry: The incoagulable nitrogen was 78 mg. per hunderd cubic centimeters of blood; uric acid nitrogen, 5.2 mg.; creatinin nitrogen 3.8 mg. per hundred cubic centimeters of blood; sugar, 0.120 per cent., and carbon dioxid 48 per cent. by volume. The Wassermann reaction of the blood and spinal fluid was negative. There was 25.2 mg. of urea nitrogen, and 0.3 mg. of uric acid nitrogen per hundred cubic centimeters of spinal fluid. The blood pressure was 190 systolic and 140 diastolic.

Course.—On admission, Aug. 15, 1920, a phlebotomy was performed immediately.

August 16: The general condition was improved. The sensorium was clear. The blood pressure was 190. Phenolsulphonephthalein excretion was 5 per cent. in two hours, and the dye was still present in the urine eleven hours later.

August 18: There had been no convulsions since admission. The vision was improving.

TABLE 2.—*Chemical Examination of Blood Before and After Transfusion*

	Before Transfusion, Mg.*	Two Days After Transfusion, Mg.*
Incoagulable nitrogen	109.0	87.0
Urea nitrogen	60.0	56.0
Uric acid	5.6	6.0
Creatinin	4.0	5.0

* Per hundred cubic centimeters of blood.

Ophthalmologic examination (Dr. Wolff): The left disk showed tremendous papilledema. The swelling was at least five diopters. At the same time, the disk was very pale, probably because of the intense anemia. A large group of glistening white spots was situated at the outer side of the disk. There were no hemorrhages. The right fundus was similar to the left, except that the swelling was less.

Blood examination: Hemoglobin was 20 per cent.; the polymorphonuclear cells, 90 per cent., with lymphocytes, 10 per cent. The blood smear showed a moderate anisocytosis and poikilocytosis. A transfusion of 12 ounces (355 c.c.) of blood, with a previous withdrawal of 8 ounces (236 c.c.) was performed. The systolic blood pressure before the transfusion was 212, but after the withdrawal of the 8 ounces was 184. With the introduction of 200 c.c. of blood, the pressure rose to 192, and immediately after the completion of the transfusion (a total of 370 c.c. of blood), the blood pressure was 200. Table 2 shows the results of the chemical examination of the blood before and after transfusion.

The total quantity of urine the day before transfusion was 1,040 c.c., with an incoagulable nitrogen content of 0.14 gm., and a sodium chlorid content of 2.57 gm.

The water test of 500 c.c. gave the results shown in Table 3.

The total urine in the first four hours was 190 c.c.; total night urine, 560 c.c., and total twenty-four hour volume, 700 c.c.

This water test shows clearly that the total quantity excreted was greater than the amount ingested, even though the amount ingested was very small; that the amount in the first four hours did not by any means equal the intake,

and that the night urine exceeded the intake, although the fluid ingested was given at 8 a. m. In addition, it was demonstrated that, with the low excretion in the first four hours there was a fixation of specific gravity, and, even with the nocturia, this fixation was still present.

August 19: Intravenous phenolsulphonephthalein administration revealed only 5 per cent. excretion of the dye in two hours. The hemoglobin was 23 per cent.

August 28: The child was doing comparatively well. The hemoglobin was 31 per cent.; the blood pressure was 178.

September 12: The child was comfortable, and out of bed and about the ward.

September 25: The patient was in fairly good condition. The hemoglobin was 45 per cent., and the blood pressure was 215. The child began to have general convulsions, which kept up for the entire day, and semicoma continued for a few days.

December 15: The child's general condition again improved. There had been no convulsions for two months. There was a hemoglobin of 40 per cent. The systolic blood pressure was about 200. The urine examination revealed traces of albumin, with occasional hyaline casts. The patient was discharged from the hospital against advice, but was observed in her home. She was readmitted, Feb. 21, 1921, two months later. During the interval, she had been free from convulsions, but she became weaker and more anemic. She died

TABLE 3.—*Water Test*

	Hour									
	8:30 a.m.	9:00 a.m.	9:30 a.m.	10:00 a.m.	10:30 a.m.	11:30 a.m.	Total	8:00 p.m.	6:00 a.m.	8:00 a.m.
Volume (c.c.)	70	25	20	15	25	35	190	170	240	150
Specific gravity	1.010	1.008	1.006	1.006	1.010	1.011		1.010	1.009	1.011

a few days after her readmission. Two days before death, a chemical examination of the blood showed urea nitrogen 61 mg. per hundred cubic centimeters of blood; uric acid nitrogen, 2.5 mg., and creatinin nitrogen, 4.2 mg.

Necropsy was not permitted.

ETIOLOGY

From a study of the histories and the course of these cases, it is impossible to ascribe any one definite causative factor. One patient had had scarlet fever, but in the others there was no history of infectious diseases. Alcohol, tobacco or a metallic poison could be excluded.

In Case 1, the patient had the wrinkled, wizened appearance associated with renal infantilism, described so well by the English authors, Miller and Parsons [2] and others. The previous history was unsatisfactory and, since the child was only 3½ years of age, it was impossible to state how long his general condition had been below normal, and just what his growth impulse was during his short span of life. Careful abdominal examination seemed to exclude the presence of congenitally cystic kidneys, and the absence of marked nitrogen

2. Miller, L., and Parsons, L.: Brit. J. Child. Dis. **9**, July, 1912.

retention seemed to exclude a marked malformation of the kidney; for it has been our experience that surgical conditions of the kidney, such as infective hydronephroses and various congenital malformations give a much higher nitrogen retention, in the hundreds of milligrams of nitrogen per hundred cubic centimeters of blood, than do the ordinary medical diseases of the kidney.

Necropsy in Case 2 disclosed that one kidney was practically absent, and that the other, although slightly larger than normal, was badly diseased. In spite of this, the growth and nutrition of the child were excellent. From this case and many others described in the literature of the subject, it can be seen that there is a congenital element in many of these cases, the remaining kidney or the deformed kidneys being insufficient to carry on the work properly; or perhaps, as Pepper and Lucke [3] have suggested, the one apparently normal kidney is especially prone to chronic inflammatory processes.

Case 3 presented the cardinal symptoms of this group, yet was essentially different in two important particulars. First, there was much less arterial thickening; secondly, there was a profound secondary anemia. Without a postmortem examination, it was impossible to say how much arteriosclerosis was present, but clinically it seemed to be much less than in the other two cases. A certain number of cases in this group, then, had an underlying congenital basis; others have a hereditary predisposition, as shown in the cases described by Brill and Libman.[4]

SYMPTOMS AND COURSE

All three cases were characterized by a rapid course, and, although the exact length of time cannot be definitely stated, all died within a year after the onset of any noticeable symptoms. Volhard [5] has described a bland, or slowly progressing, form of hypertension nephritis (contracted kidney or *Schrumpfniere*) and a malignant, rapidly progressing form. In the former, there is no kidney insufficiency nor are there cardiac symptoms, but a slowly increasing hypertension. From my experience and from the study of the literature, these cases must be very rare in infancy and childhood. The malignant form of the adult has much in common with the group we are describing. Yet, the underlying etiologic factors, such as congenital anomalies and hereditary influences, which appear in many cases to be a dominant feature of this condition in children, prevent us from describing this

3. Pepper, O. H. P., and Lucke, Baldwin: Fatal Chronic Nephritis in a Fourteen Year Old Girl with Only One kidney and a History of Scarlet Fever, Arch. Int. Med. **27**:661 (June) 1921.

4. Brill, N., and Libman, E.: J. Exper. Med. **4**:541, 1899.

5. Volhard, F.: Die Doppelseitigen Hematogenen Nierenerkrankungen, Julius Springer, 1918.

group as one of primary contracted kidney. It has therefore seemed best to us to group them as cases of malignant hypertension nephritis, with varying anatomic and heritary causes.

The subjective symptoms seemed very vague until the kidney insufficiency was far advanced; for there was relatively little history of complaint, except perhaps of a general feeling of weakness and malaise. Headache and vomiting were not prominent features until the condition was well advanced. Most interesting and important, and present in all three cases, was the marked abdominal pain. This pain came on at about the same time that the urinary disturbances were noticed, but the pain was the chief complaint in all three cases. So pregnant was this symptom that, when the second and third cases were admitted to the hospital, blood pressure and eyeground examinations were immediately made, and the true condition was discovered. The exact cause of this pain could not be determined; yet it had a marked resemblance to the "abdominal angina" that adults with hypertension have. In Case 2, necropsy revealed an intussusception; yet this could not have been the cause of the pain of about four months' duration, for the intussusception seemed to be of recent origin. Drugs producing arterial dilatation had no effect on the pain.

The growth and nutrition of the second and third patients were all that could be desired. But it seemed that Case 1 might be placed in the category of renal infantilism. Unfortunately, we could not obtain a necropsy, so the type of lesion could not be determined.

The kidney function in all cases, as shown by an examination of the urine and of the blood, was profoundly disturbed. The urinary output was greater than the absolute fluid intake. There were polyuria and fixation of specific gravity at a low level, and a slight amount of albumin and a small number of hyaline and granular casts were present in the urine. A chemical examination of the blood for its nitrogenous constituents showed that, in one case, there was a very moderate increase of the nitrogenous elements in the blood. Case 2, however, showed marked retention of nitrogen, and as it proved, presented a congenital lesion. It is a temptation to deduce from this that our first case had no congenital deformity; yet we are loath to do so, for our experience is as yet too small.

The phenolsulphonephthalein output was only moderately diminished in Case 1, but in Case 3 it was almost nil, even when the drug was given intravenously.

The hypertension in these cases was marked and constant, both the systolic and diastolic pressures being greatly increased. This is hardly the place to go into a discussion as to the cause of the hypertension, whether primary or secondary to the kidney lesion, or whether due

to an extrarenal poisoning affecting the capillaries of the body. The action of this poison must have been different in our last case, for the arterial thickening was absent and anemia was marked.

Clinical examination of the blood showed no anemia in the first and second cases, although there was marked nitrogen retention in the latter. So nitrogen retention alone cannot account for the severe anemia which was present in our third case. This would bear out the observations made by Brown and Roth [6] at the Mayo Clinic. According to Volhard, there is often a polycythemia in the primary contracted kidney, and an anemia in the secondarily contracted kidney.

The ophthalmologic findings were characteristic of these cases, and similar to those found in the last stages of hypertension nephritis in the adult. There was a marked albuminuric retinitis present in all cases, which, according to Volhard, is supposed to be due to the constantly high blood pressure and the consequent ischemic condition of the retina.

The heart in all our cases showed a moderate hypertrophy of the left ventricle. The blood vessels in the case that came to necropsy showed marked arteriosclerosis.

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6. Brown, G. E., and Roth, Grace M.: Anemia of Chronic Nephritis, Arch. Int. Med. **30**:817 (Dec.) 1922.

STUDIES IN THE URIC ACID METABOLISM OF CHILDREN *

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There is, perhaps, no nitrogenous substance in the urine that has been more carefully studied than uric acid. The majority of the investigations concerning the uric acid content of the urine which have been carried out have dealt chiefly with adults. The present report is of a study of the uric acid metabolism in children.

It was believed for a long time that uric acid in mammalian urine was an intermediary product of protein metabolism which was almost completely oxidized by the body to urea. We now know that this point of view is fundamentally incorrect, and that uric acid is derived from the catabolism of the nucleins of both the food and the tissues. As is well known, the nucleins contain nucleic acid, which in turn contains purins. It is the oxidation of the purins that yields uric acid.

The variations in the total daily elimination of uric acid, following different diets, varying states of health and individual idiosyncrasies, have been determined by numerous investigators. The fact that purins are found in the urine during starvation and on a purin-free diet has led to considerable investigation, in a search for some source for purins within the organism, beside that of ingested nucleins. Burian and Schur,[1] who were the first to distinguish clearly between exogenous and endogenous uric acid, maintained that while the endogenous fraction of uric acid might show variation depending on individual differences, the amount eliminated by one individual remained fairly constant, and the quantity was not altered by the intake of purin-free food.

Other investigators, Siven,[2] Hall,[3] Brugsch and Schittenhelm,[4] have also emphasized the fact that the output of endogenous uric acid during the twenty-four hour period is constant for one person, but the fact that the endogenous uric acid is not altered by the intake of purin free

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1. Burian, R., and Schur, H.: Arch. f. d. ges. Physiol. **87**:239, 1901.
2. Siven, V. O.: Skandin. Arch. f. Physiol., Leipzig. **11**:123, 1901.
3. Hall, I. W.: The Purin Bodies of Foodstuffs, Manchester, Sherratt and Hughes, 1902.
4. Brugsch, T., and Schittenhelm, A.: Der Nukleinstoffwechsel und seine Storungen, Jena, G. Fischer, 1910.

food has not been accepted. Mares,[5] Taylor and Rose,[6] Hopkins and Hope,[7] Smetanka,[8] Lambling and Dubois,[9] Folin,[10] Mendel and Stehle,[11] have demonstrated that the ingestion of food free from purin precursors, particularly the proteins, may, in any person, markedly raise the level of endogenous uric acid excretion. Mares suggests that this may be the results of the wear and tear on the nuclear material of the secretory glands of the gastro-intestinal tract, brought about by the work of secretion occasioned by the presence of food in the alimentary tract; though Lewis [12] and his co-workers are not of this opinion. The latter investigators suggest that the effect may be due to a general stimulation of all cellular metabolism by amino-acids, products of protein metabolism, a theory which has been fully discussed by Rose,[13] who has given further evidence to support it. Hermann,[14] in studying the effect of adding to a normal mixed diet fat in the form of butter, noticed a diminished output of uric acid, but concluded that fat had no effect on uric acid elimination. Umeda [15] found that on a fat-rich, carbohydrate-poor diet the excretion of uric acid was diminished, but attributed the effect to the acidosis occasioned by the lack of carbohydrates. Horbaczewski and Kanera,[16] who added 100 gm. of fat to a high protein diet, observed a slight decrease in the uric acid elimination, which they attributed to a weak protein sparing action of the fats. Lewis and Corley [17] could not demonstrate any influence on the hourly elimination of uric acid in the fasting individual, after the administration of fat (cream) in amounts up to approximately 135 gm. Smetanka found an increased excretion of uric acid after the ingestion of large amounts of honey (from 200 to 300 gm.) and potatoes (from 375 to 450 gm.), an effect thought by them to be due to the increased activity of the liver cells in the formation of glycogen. Lewis and Corley found that lactose, sucrose and glucose in moderate amounts (100 gm.) did not influence uric acid elimination, though honey and commercial glucose syrup in amounts greater than 200 gm. caused increased elimination. This increase, however, was neither as constant nor as marked as that which followed the

5. Mares, F.: Arch. slav. Biol. **3**:207, abstr., Centralbl. f. d. med. Wissensch. **26**:2, 1888.
6. Taylor, A. E., and Rose, W. C.: J. Biol. Chem. **18**:519, 1914.
7. Hopkins, F. G., and Hope, W. B.: J. Physiol. **23**:271, 1898-1899.
8. Smetanka, F.: Arch. f. d. ges. Physiol. **138**:217, 1911.
9. Lambling, E., and Dubois, F.: Compt. rend. Soc. de biol. **76**:614, 1914.
10. Folin, O.: Am. J. Physiol. **13**:66-117, 1905.
11. Mendel, L. B., and Stehle, R. L.: J. Biol. Chem. **22**:215, 1915.
12. Lewis, H. B.; Dunn, M. S., and Doisy, E. A.: J. Biol. Chem. **36**:19 (Oct.) 1918.
13. Rose, W. C.: J. Biol. Chem. **48**:563-565 (Oct.) 1921.
14. Hermann, A.: Deutsch. Arch. f. klin. Med. **43**:273, 1888.
15. Umeda, N.: Biochem. J. Lond. **9**:38, 1915.
16. Horbaczewski, J., and Kanera F.: Monatschr. Chem. **7**:105, 1886.
17. Lewis, H. B., and Corley, R. C.: J. Biol. Chem. **55**:273 (March) 1923.

ingestion of amino-acids or glycerin. According to Höst,[18] an increase in caloric intake beyond a certain minimum increases the endogenous uric acid, and the greater increase is, in his opinion, due to the protein intake. Neuwirth,[19] who confirmed the results obtained by Mendel and Stehle, showed that within certain limits there was a relationship between urinary volume and uric acid excretion, and that as a rule a decrease in urinary output meant a decrease in uric acid elimination, and further that a marked fall in the uric acid output occurred during the morning hours, and was followed by a further gradual decline during the afternoon.

METABOLIC STUDIES

Our studies were made on five normal children, who were kept under careful observation in the hospital wards. The uric acid metabolism was investigated under varying conditions, the general plan of which is here briefly presented: There was, in all instances, a preliminary period during which a weighed mixed purin-free diet was administered. This was followed by a period, during which measured amounts of water and four bran muffins were allowed. In the third period, the diet was high in carbohydrates and low in fats, while in the fourth period it was rich in proteins and low in carbohydrates and fats. In the fifth period, the fat content was high and the protein and carbohydrate low. All these diets were purin-free. The duration of each period varied from two to four days and the order in which they were introduced differed in each case. This was done in order to determine whether the same results would be obtained regardless of the order in which the dietary periods were introduced. Each day, at approximately the same time, the patients were weighed, and on the second day of each period, at approximately the same time, chemical examinations of the blood (urea nitrogen, van Slyke and Cullen method; creatinin and sugar, Myers and Fine method; uric acid, Benedict[20] method) were made, with the patient in a fasting condition. The caloric value of each diet was noted; the fluid intake and output for each twenty-four hour period was determined, and the total uric acid elimination was estimated (Benedict[21] method). For one or two days of each period, a measured amount of uric acid was given by mouth, and for at least one day in each period the uric acid elimination in the urine was estimated at two hour intervals.

REPORT OF CASES

CASE 1 (Tables 1, 2, 3).—H. S., aged 8 years, observed for a period of nineteen days, during the first four days was given a mixed purin-free diet

18. Höst, H. F.: J. Biol. Chem. **38**:17 (May) 1919.
19. Neuwirth, I.: J. Biol. Chem. **29**:477 (April) 1917.
20. Benedict, S. R.: J. Biol. Chem. **51**:187 (March) 1922.
21. Benedict, S. R., and Franke, E.: J. Biol. Chem. **52**:387 (June) 1922.

consisting of protein, 80 gm.; fat, 94 gm.; carbohydrate, 54 gm. To this, on the second and third day, 1 gm. of uric acid was added, and blood chemistry determinations were made on the second day. A three-day period followed, during which the diet consisted of a measured amount of water and four bran muffins. On the second and third day of this period, 1 gm. of uric acid was given by mouth, and chemical examinations of the blood were made on the second day.

TABLE 1 *(Case 1).—Summary of Findings: Chronic Cervical Adenitis*

Date	Diet	Protein	Fat	Carbohydrate	Calories	Body Weight, Kg.	Intake, C.c.	Output, C.c.	Uric Acid Excretion, Mg.	Uric Acid Feeding
9/21	Mixed, normal	80	94	54	1,424	24.5	1,200	1,100	260	None
9/22*	Normal	80	94	54	1,424	24.5	1,200	1,180	277	1 gm.
9/23	Normal	80	94	54	1,424	24.5	1,200	1,170	300	1 gm.
9/24	Normal	80	94	54	1,424	24.2	1,200	1,035	325	None
9/25	Fasting	0	0	0	0	23.9	1,000	900	228	None
9/26*	Fasting	0	0	0	0	23.6	1,000	950	194	1 gm.
9/27	Fasting	0	0	0	0	23.1	1,000	980	113	1 gm.
9/28	High carbohydrate	19	7	303	1,385	23.1	1,100	1,020	260	None
9/29*	High carbohydrate	19	7	303	1,385	23.3	1,200	1,130	265	1 gm.
9/30	High carbohydrate	19	7	303	1,385	23.4	1,200	1,184	230	1 gm.
10/ 1	High carbohydrate	19	7	303	1,385	23.7	1,200	1,030	242	None
10/ 2	High fat	9	150	11	1,477	23.6	1,100	1,048	119	1 gm.
10/ 3*	High fat	9	150	11	1,477	23.2	1,200	1,156	112	1 gm.
10/ 4	High fat	9	150	11	1,477	23.1	1,200	1,120	115	None
10/ 5	Normal	80	94	54	1,424	23.4	1,200	1,110	247	None
10/ 6*	Normal	80	94	54	1,424	23.6	1,200	1,140	273	1 gm.
10/ 7	High protein	148	13	68	1,007	23.7	1,600	1,540	358	None
10/ 8*	High protein	148	13	68	1,007	23.9	1,600	1,560	388	1 gm.
10/ 9	High protein	148	13	68	1,007	24.1	1,600	1,545	390	1 gm.

* Days on which blood chemistry determinations were made.

TABLE 2 *(Case 1).—Blood Chemistry Determinations*

Date	Urea Nitrogen, Mg. per 100 C.c.	Creatinin, Mg. per 100 C.c.	Uric Acid, Mg. per 100 C.c.	Sugar, Mg. per 100 C.c.
9/22	17.0	0.5	2.3	80
9/26	18.0	0.5	2.5	84
9/29	16.5	0.7	2.2	82
10/ 3	15.0	0.8	2.1	90
10/ 6	16.0	0.7	2.4	85
10/ 8	17.0	0.8	2.8	90

TABLE 3 *(Case 1).—Changes in Blood Chemistry Following Ingestion of Uric Acid During High Protein Period (Amount Given, 1 Gm., at 9 a. m.)*

Date	Diet	Time		Mg. per 100 C.c. Blood			
		A.M.	P.M.	Creatinin	Urea Nitrogen	Uric Acid	Sugar
10/9	High protein	9:30		0.8	17.0	2.9	80
		11:00		0.9	16.0	2.5	100
		12:00		—	15.0	3.0	—
			1:00	—	14.0	2.8	—
			2:00	—	14.5	2.7	—

For the next four days, a high carbohydrate diet was given, consisting of protein, 19 gm.; fat, 17 gm.; carbohydrate, 303 gm. The same uric acid feeding and chemical examinations of the blood were made as in the previous periods. Following this was a three-day period of a high fat diet consisting of protein, 9 gm.; fat, 150 gm.; carbohydrate, 11 gm.; 1 gm. of uric acid being given on the first and second days.

This period was followed by two days of a mixed purin-free diet similar to that of the first period, 1 gm. of uric acid being administered on the second day.

The diet of the last period was a high protein one consisting of protein, 148 gm.; fat, 13 gm.; carbohydrate, 68 gm., and again 1 gm. of uric acid was given on the second and third days. The blood chemistry determinations were made on the second day. The data of the various determinations are shown in Table 2.

On the last day of the above-mentioned period, 1 gm. of uric acid was given at 9 a. m. Chemical examinations of the blood were made at 9:30, 11 and 12 a. m., and at 1 and 2 p. m., to ascertain whether any changes occurred in the blood following the ingestion of uric acid. These results are given in Table 3.

CASE 2 (Tables 4, 5, 6).—A. T., aged 10 years, was observed over a period of sixteen days. The arrangement of the various dietary periods is noted in Table 4, and is similar to that of Case 1, except for the order in which the

TABLE 4 *(Case 2).—Summary of Findings: Chorea*

Date	Diet	Protein	Fat	Carbohydrate	Calories	Body Weight, Kg.	Intake, C.c.	Output, C.c.	Uric Acid Excretion, Mg.	Uric Acid Feeding
10/16	Mixed	65	80	60	1,257	23.2	800	760	268	None
10/17*	Normal	65	80	60	1,257	23.3	900	820	234	1 gm.
10/18	Starvation	0	0	0	0	23.0	960	900	190	None
10/19*	Starvation	0	0	0	0	23.0	985	900	125	1 gm.
10/20*‡	Normal	80	90	75	1,473	23.4	1,000	940	243	None
10/21‡	Normal	80	90	75	1,473	23.6	1,100	1,080	229	1 gm.
10/22	High fat	8	200	10	2,188	23.2	900	850	195	None
10/23*	High fat	8	200	10	2,188	23.0	1,000	975	180	1 gm.
10/24	High fat	8	200	10	2,188	23.0	1,000	980	175	1 gm.
10/25	High carbohydrate	15	8	280	1,284	23.1	1,000	985	205	None
10/26*	High carbohydrate	15	8	280	1,284	23.1	1,000	985	234	1 gm.
10/27	High carbohydrate	15	8	280	1,284	23.3	1,000	995	230	1 gm.
10/28	High protein	250	12	7	1,155	23.3	1,000	990	265	None
10/29	High protein	250	12	7	1,155	23.4	1,000	994	273	1 gm.
10/30*	High protein	250	12	7	1,155	23.5	1,000	986	295	1 gm.
10/31	Normal	80	90	75	1,473	23.5	1,000	990	247	None

* Days on which blood chemistry determinations were made.
‡ Collection of urine in two hourly periods during the day.

TABLE 5 *(Case 2).—Blood Chemistry Determinations*

Date	Urea Nitrogen, Mg. per 100 C.c.	Creatinin, Mg. per 100 C.c.	Uric Acid, Mg. per 100 C.c.	Sugar, Mg. per 100 C.c.
10/17	14.3	1.7	2.5	94
10/19	15.2	1.5	2.4	91
10/20	14.4	1.6	2.3	93
10/23	12.8	1.6	2.4	98
10/26	12.9	1.7	2.3	96
10/30	12.8	1.8	2.6	91

TABLE 6 *(Case 2).—Two Hourly Excretion of Uric Acid*

Date	Diet: Protein	Diet: Fat	Diet: Carbohydrate	Time	Urine Output, C.c.	Uric Acid Excretion, Mg.
10/20	80	90	75	A.M. P.M. 10:30-12:30	240	60.0
				2:30	165	33.5
				4:30	50	27.3
				6:30	90	19.2
				8:30	110	30.1
				P.M. A.M. 8:30-10:30	285	71.3
10/21	80	90	75	A.M. P.M. 10:30-12:30	235	45.3
				2:30	130	22.5
				4:30	75	20.0
				6:30	80	10.0
				8:30	110	25.7
				P.M. A.M. 8:30-10.30	450	105.0

periods were introduced. The two hourly excretion of uric acid was determined here for two successive days, October 20 and 21 (Table 6), the diet being a mixed purin-free one consisting of protein, 80 gm.; fat, 90 gm.; carbohydrate, 75 gm. On the second day (October 21), 1 gm. of uric acid was given. Specimens of urine were collected every two hours from 10:30 a. m. to 8:30 p. m., October 20, and one specimen from then until 10:30 a. m., October 21. The urine for the second day was similarly collected.

CASE 3 (Tables 7, 8, 9, 10).—D. D., aged 9 years, observed over a period of nineteen days, was given a mixed purin-free diet, October 31, with 1 gm. of uric acid at 9 a. m. Chemical examinations of the blood were made at 9:30, 11 and 12 a. m., and at 1 and 2 p. m. (Table 10).

TABLE 7 *(Case 3).—Summary of Findings: Chorea*

Date	Diet	Protein	Fat	Carbohydrate	Calories	Body Weight, Kg.	Intake, C.c.	Output, C.c.	Uric Acid Excretion, Mg.	Uric Acid Feeding
10/30	Mixed, normal	70	81	45	1,225	22.4	875	856	285	None
10/31*	Normal	70	81	45	1,225	22.3	900	890	261	1 gm.
11/ 1	Normal	70	81	45	1,225	22.3	900	880	264	1 gm.
11/ 2‡	Normal	70	81	45	1,225	22.5	1,200	1,124	268	None
11/ 3	Normal	70	81	45	1,225	22.4	1,000	980	235	None
11/ 4	Starvation	0	0	0	0	22.1	1,000	985	121	None
11/ 5*	Starvation	0	0	0	0	22.0	1,000	987	101	1 gm.
11/ 6	Starvation	0	0	0	0	21.8	1,000	970	100	1 gm.
11/ 7	High fat	12	110	15	1,134	21.9	1,000	986	164	None
11/ 8*	High fat	12	110	15	1,134	22.1	1,000	990	167	1 gm.
11/ 9	High fat	12	110	15	1,134	22.1	1,000	982	182	1 gm.
11/10	High protein	220	30	20	1,263	22.3	1,000	974	224	None
11/11*	High protein	220	30	20	1,263	22.5	1,000	990	287	1 gm.
11/12	High protein	220	30	20	1,263	22.7	1,000	960	305	1 gm.
11/13	Starvation	0	0	0	0	22.5	1,000	870	147	None
11/14*‡	Starvation	0	0	0	0	22.3	1,200	1,124	127.3	1 gm.
11/15	High carbohydrate	20	12	300	1,424	22.4	1,000	988	167	None
11/16*	High carbohydrate	20	12	300	1,424	22.6	1,000	970	210	1 gm.
11/17	High carbohydrate	20	12	300	1,424	22.8	1,000	910	250	None

* Days on which blood chemistry determinations were made
‡ Collection of urine in two hourly periods during the day.

TABLE 8 *(Case 3).—Blood Chemistry Determinations*

Date	Urea Nitrogen, Mg. per 100 C.c.	Creatinin, Mg. per 100 C.c.	Uric Acid, Mg. per 100 C.c.	Sugar, Mg. per 100 C.c.
10/31	15.0	1.8	3.1	108
11/ 5	14.0	1.6	2.8	98
11/ 8	15.0	1.6	2.7	96
11/11	14.0	1.5	2.6	98
11/14	14.3	1.2	2.3	104
11/16	15.0	1.5	2.8	94

TABLE 9 *(Case 3).—Two Hourly Excretion of Uric Acid*

Date	Diet: Protein	Diet: Fat	Diet: Carbohydrate	Time	Urine Output, C.c.	Uric Acid Excretion, Mg.
11/2	70	81	45	A.M. P.M. 10:30–12:30	310	53.9
				2:30	137	30.5
				4:30	125	28.0
				6:30	48	12.0
				8:30	154	37.0
				P.M. A.M. 8:30–10:30	350	107.5
				A.M. P.M.		
11/14	0	0	0	10:30–12:30	260	24.2
				2:30	180	19.0
				4:30	110	18.1
				6:30	90	14.0
				8:30	174	22.0
				P.M. A.M. 8:30–10:30	310	30.0

TABLE 10 *(Case 3).—Changes in Blood Chemistry Following Ingestion of Uric Acid, During Mixed Purin-Free Diet (Amount Given, 1 Gm., at 9 p. m.)*

Date	Diet	Time A.M.	Time P.M.	Mg. per 100 C.c. Blood: Creatinin	Urea Nitrogen	Uric Acid	Sugar
10/31	Mixed.....	9:30		1.8	15.0	3.1	108
		11:30		1.5	16.5	2.8	96
		12:00		—	16.0	3.3	—
			1:00	—	14.0	3.0	—
			2:00	—	14.0	2.9	—

CASE 4 (Tables 11, 12, 13).—B. C., aged 7 years, was observed for six days.

TABLE 11 *(Case 4).—Summary of Findings: Convalescent from Pneumonia*

Date	Diet	Protein	Fat	Carbohydrate	Calories	Body Weight, Kg.	Intake, C.c.	Output, C.c.	Uric Acid Excretion, Mg.	Uric Acid Feeding
10/16	Mixed.....	65	80	60	1,257	25.5	1,300	1,290	336.5	None
10/17*	Normal.....	65	80	60	1,257	25.3	1,300	1,200	313	1 gm.
10/18	Starvation.....	0	0	0	0	25.1	1,000	970	200	None
10/19*	Starvation.....	0	0	0	0	24.9	1,000	980	140	1 gm.
10/20‡	Normal.....	80	90	75	1,473	24.8	900	838	237	None
10/21*‡	Normal.....	80	90	75	1,473	24.9	1,100	1,022	228	1 gm.

* Days on which blood chemistry determinations were made.
‡ Collection of urine in two hourly periods during the day.

TABLE 12 *(Case 4).—Blood Chemistry Determinations*

Date	Urea Nitrogen, Mg. per 100 C.c.	Creatinin, Mg. per 100 C.c.	Uric Acid, Mg. per 100 C.c.	Sugar, Mg. per 100 C.c.
10/17.....	16.5	0.5	3.0	82
10/19.....	15.0	0.7	3.2	90
10/21.....	18.0	0.6	3.0	84

TABLE 13 *(Case 4).—Two Hourly Excretion of Uric Acid*

Date	Diet: Protein	Fat	Carbohydrate	Time: A.M. P.M.	Urine Output, C.c.	Uric Acid Excretion, Mg.
10/20.....	80	90	75	10:30–12:30	239	59.8
				2:30*	90	28.4
				4:30	52	26.0
				6:30	31	18.0
				8:30	170	32.0
				P.M. A.M.		
				8:30–10:30	256	73.0
				A.M. P.M.		
10/21.....	80	90	75	10:30–12:30	255	30.6
				2:30	106	24.5
				4:30	91	21.0
				6:30	61	18.3
				8:30	79	27.0
				P.M. A.M.		
				8:30–10:30	430	107.5

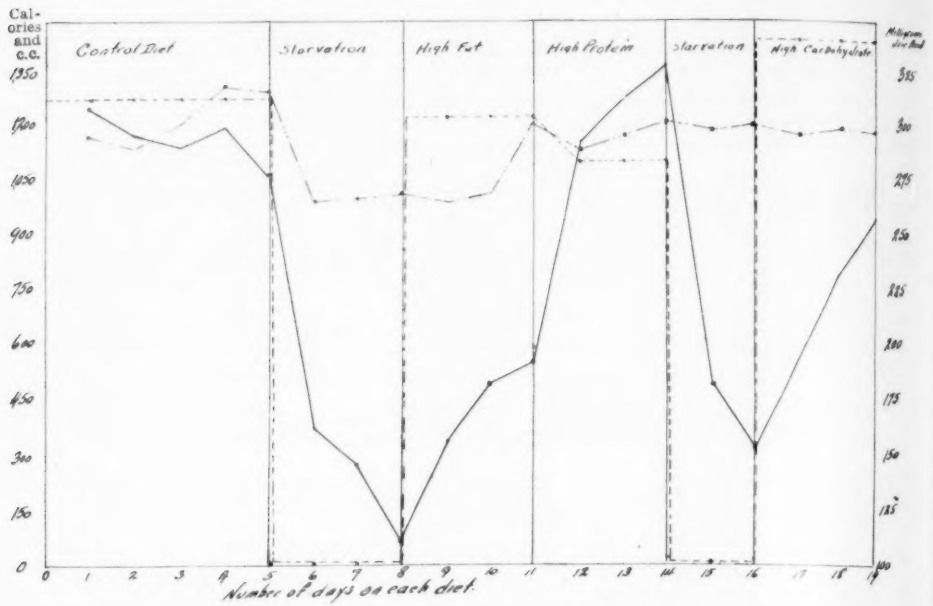

Chart 1 (Case 5).—Relationship between (*a*) uric acid excretion and caloric intake; (*b*) uric acid excretion and water output; straight line, uric acid excretion; broken line, caloric intake; dot and dash line, water output.

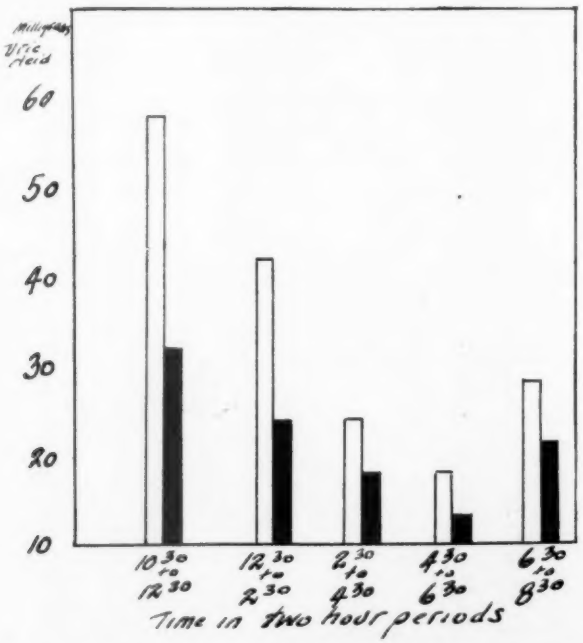

Chart 2 (Case 5).—Two hour periods of uric acid excretion on control diet and starvation; control, white; starvation, black.

CASE 5 (Tables 14, 15, 16).—A. W., aged 12 years, was studied for nineteen days. The procedure was similar to that in the other cases.

TABLE 14 *(Case 5).—Summary of Findings: Chorea*

Date	Diet	Protein	Fat	Carbohydrate	Calories	Body Weight, Kg.	Intake, C.c.	Uric Acid Output, C.c.	Uric Acid Excretion, Mg.	Uric Acid Feeding
10/30	Mixed, normal	90	70	60	1,260	33.2	1,200	1,160	305	None
10/31*	Mixed	90	70	60	1,260	33.2	1,200	1,120	294	1 gm.
11/ 1	Mixed	90	70	60	1,260	33.1	1,280	1,190	288	None
11/ 2‡	Mixed	90	70	60	1,260	33.0	1,300	1,293	296	None
11/ 3	Mixed	90	70	60	1,260	33.1	1,300	1,285	275	None
11/ 4	Starvation	0	0	0	0	32.9	1,000	985	160	None
11/ 5*	Starvation	0	0	0	0	32.7	1,000	990	145	1 gm.
11/ 6	Starvation	0	0	0	0	32.6	1,000	994	110	None
11/ 7	High fat	10	120	12	1,206	32.5	1,000	984	155	None
11/ 8*	High fat	10	120	12	1,206	32.2	1,000	992	180	1 gm.
11/ 9	High fat	10	120	12	1,206	32.2	1,200	1,180	190	None
11/10	High protein	200	15	30	1,083	32.3	1,200	1,120	290	None
11/11*	High protein	200	15	30	1,083	32.5	1,200	1,165	310	1 gm.
11/12	High protein	200	15	30	1,083	32.5	1,200	1,180	325	None
11/13	Starvation	0	0	0	0	32.4	1,200	1,170	180	None
11/14*‡	Starvation	0	0	0	0	32.4	1,200	920	152	1 gm.
11/15	High carbohydrate	15	10	320	1,467	32.5	1,200	1,160	190	None
11/16*	High carbohydrate	15	10	320	1,467	32.7	1,200	1,175	230	1 gm.
11/17	High carbohydrate	15	10	320	1,467	32.9	1,200	1,170	255	None

* Days on which blood chemistry determinations were made.
‡ Collection of urine in two hourly periods during the day.

TABLE 15 *(Case 5).—Blood Chemistry Determinations*

Date	Urea Nitrogen, Mg. per 100 C.c.	Creatinin, Mg. per 100 C.c.	Uric Acid, Mg. per 100 C.c.	Sugar, Mg. per 100 C.c.
10/31	14.8	1.4	2.5	102
11/ 5	13.4	1.8	2.1	108
11/ 8	12.5	1.6	2.1	96
11/11	15.2	1.8	2.7	98
11/14	14.7	1.6	2.5	96
11/16	14.8	1.5	2.3	94

TABLE 16 *(Case 5).—Hourly Excretion of Uric Acid*

Date	Diet: Protein	Diet: Fat	Diet: Carbohydrate	Time	Urine Output, C.c.	Uric Acid Excretion, Mg.
11/2	90	70	60	A.M. P.M. 10:30-12:30	350	58
				2:30	248	42
				4:30	110	24
				6:30	70	20
				8:30	95	28
				P.M. A.M. 8:30-10:30	424	124
11/14	0	0	0	A.M. P.M. 10:30-12:30	230	32
				2:30	140	24
				4:30	115	18
				6:30	65	13
				8:30	70	21
				P.M. A.M. 8:30-10:30	300	44

BLOOD CHANGES IN THE URIC ACID METABOLISM

Tables 2, 5, 8, 12 and 15 show the results of chemical blood examinations made while the patients were kept on the different dietary regimens outlined at the beginning of the paper. A study of these tables reveals that the variations in the different blood constituents were very slight, particularly for the uric acid, and for all practical purposes may be disregarded.

When uric acid was fed and blood determinations were made at repeated intervals thereafter, only slight changes in the uric acid content of the blood were noted, in the two cases in which such examinations were made (Case 1, Table 3, and Case 3, Table 10). In Case 1, a high protein diet was allowed. At 9 a. m., 1 gm. of uric acid was fed to the patient and chemical examinations of the blood were made at 9:30, 11, 12 a. m. and also at 1 and 2 p. m. The blood uric acid at these intervals was 2.9, 2.5, 3.0, 2.8 and 2.7 mg., respectively. In Case 3, a mixed purin-free diet was allowed, while the rest of the procedure was the same as in Case 1. The blood uric acid at these intervals was 3.1, 2.8, 3.3, 3.0 and 2.9 mg. Whether these slight variations are of any significance is doubtful.

EFFECT OF DIFFERENT PURIN-FREE DIETS ON THE DAILY URIC ACID OUTPUT

As the results obtained were practically identical in the cases studied, one of the group will serve for the purposes of specific discussion. The data in each case may be obtained by reference to Tables 1, 4, 7, 11 and 14. Table 4 shows that on a mixed purin-free diet, the uric acid excretion for the twenty-four hour period was 268 mg. the first day and 234 mg. the second. This dietary period was considered the control period in our cases.

On the starvation diet the uric acid excretion fell to 190 mg. the first day and to 125 mg. the second. When the control diet was resumed, the twenty-four hour excretion rose to 243 mg., and on the following day was 229 mg. These figures are of interest because they show an increase in the uric acid excretion after the administration of food free from purins.

On a high fat diet, the uric acid excretion was considerably lower than that obtained on the mixed purin-free diet, and but slightly greater than that observed during the starvation period. In Case 2, the twenty-four hour excretion on the three successive days of the high fat diet dropped to 195, 180 and 175 mg. It will be noted that the sudden fall is similar to that observed during the starvation period. Evidently, the high fat diet has an inhibiting effect on the excretion of uric acid. This

observation agrees with the results obtained by Hermann and Horbaczewski and Kanrera, but does not support the claims of Lewis and Corley.

While the caloric value of the high fat diet employed in Case 2 is higher than that of the other diets, its effect on uric acid excretion is almost the same as that of starvation. This is of interest since Höst found that an increase in the caloric intake beyond a certain minimum gave rise to an increase in the endogenous uric acid. The curve of excretion and its relation to caloric intake can be more readily comprehended by references to Chart 1, in which the numerical data in Case 5 are graphically shown.

During the three days of the high carbohydrate diet employed in Case 2, the uric acid excretion was 205, 234, and 230 mg. These results are almost the same as those obtained during the mixed purin-free diet period. In other cases, the excretion of uric acid was even less than that observed with the control diet. These results seem to be in opposition to those of Smetanka, who found that the uric acid excretion was increased after the administration of carbohydrates. However, they confirm the work of Lewis and Corley.

In all of the cases studied, a sharp rise in the uric acid output was noted immediately on the intake of a high protein diet, which was higher than that obtained on a mixed purin-free diet. In Case 2, the values were 265, 273 and 295 mg., respectively, for the three days. These results seem to be in accord with those obtained by other investigators, who have demonstrated that high protein diets raise the level of endogenous uric acid excretion, probably as the result of the catabolism of the nucleoproteins of the body tissues, which, as has been suggested by Lewis, may in part be aided by cellular metabolic stimulation from the amino-acids derived from the proteins. While a high protein diet is a factor in the increased elimination of uric acid, it cannot be regarded as a quantitative one, for the protein ingestion in Case 2 was almost four times as much as that of the control diet; whereas, the uric acid excretion was only about one-tenth greater than that observed with the control diet. A possible explanation may be that a slight increase of protein is sufficient to stimulate the organism to increased purin metabolism, and that further addition of protein increases the amount of uric acid elimination up to a point which may be termed the limit of protein action. Beyond this, an additional intake of protein is without appreciable effect on the uric acid elimination.

VARIATIONS IN THE URIC ACID ELIMINATION THROUGHOUT THE TWENTY-FOUR HOUR PERIOD

This phase of the problem was investigated in Cases 2, 3, 4 and 5, the results being recorded in Tables 6, 9, 13 and 16. In Cases 2 and 4,

the two hourly excretion of uric acid was determined on two separate days, on a mixed purin-free diet. Cases 3 and 5, the examinations were made during the administration of a mixed purin-free diet and during a starvation period.

Table 6 shows the excretion to be highest between 10 and 12 in the morning, followed by a progressive fall until the minimum is reached at 6:30 in the evening, with a rise again at the 8 p. m. period. Neuwirth has reported similar findings, although he did not call particular attention to this fact. That the urinary volume has any bearing on this curve of elimination cannot be determined from the findings in our cases, although Neuwirth found that a decrease in water output was generally followed by a decrease in uric acid excretion. Our results do not confirm this statement. It will be noted that the output on the first day at 4:30 in the afternoon was 50 c c. and the uric acid excretion 27.3 mg., while at 6:30 p. m., the volume was 90 c c. and the uric acid only 19.2 mg. A more complete idea of the relation between urinary volume and uric acid excretion may be obtained by reference to Chart 1.

Why the uric acid excretion should be higher at 10:30 a. m. than at any other time of the day cannot be entirely explained by the increased urinary output; nor can it be attributed to the fact that this high period occurs after feeding, as the greatest decrease is observed directly after the evening meal, which was given at 5:30 p. m. We do not offer any explanation for this peculiar phenomenon of increased morning uric acid elimination.

SUMMARY

1. The uric acid elimination for the twenty-four hour period remained fairly constant for the same person, while on a mixed purin-free diet.

2. During the fasting condition, the uric acid elimination for the twenty-four hour period reaches a minimum, and averages approximately one third of the amount eliminated on a mixed purin-free diet.

3. A high protein diet results in a greater uric acid elimination than does a purin-free diet.

4. A diet high in carbohydrates does not result in a greater uric acid elimination, beyond that observed after a mixed purin-free diet.

5. A high fat diet produces a marked diminution in the uric acid elimination when compared with the amount eliminated on a mixed purin-free diet, and this amount is slightly higher than that eliminated during the fasting condition.

6. A study of the two hourly excretion of uric acid shows a high morning elimination, with a gradual decrease throughout the day, reaching a minimum late in the afternoon, with a slight secondary rise in the evening.

7. There is no relationship between the amount of uric acid eliminated and the total urinary output.

8. The uric acid elimination does not bear any relationship to the total caloric value of diet.

9. The feeding of uric acid does not influence the amount of uric acid eliminated in the urine.

10. The administration of uric acid does not influence the concentration of uric acid in the blood.

11. The blood concentrations of urea nitrogen, uric acid, creatinin and sugar remain unchanged regardless of the type of diet.

MEASLES TRANSMITTED BY BLOOD TRANSFUSION*

REPORT OF A CASE

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Much experimental work has been done on the transmission of infectious disease and the results are generally accepted. Experimental work, as a rule, is done on animals, and we assume that man reacts in a similar manner. Since infectious disease of man is common, we are interested to know how long the infection may be in his body before physical signs are present.

The transmission of measles has been studied for many years and clinical observation of cases has given much information. Because such observations could not explain certain details, Home of Edinburgh, in 1758, was prompted to attempt to produce measles experimentally, and since then many workers have attempted to produce this disease in various ways.

Hektoen [1] has reviewed the literature on transmission of measles to January, 1905. He collected blood early in measles, cultured it on ascites broth and then injected 4 c.c. under the skin of a healthy person. On the thirteenth day after injection, the temperature rose to 101 F.; on the fourteenth day, it rose to 103 F., and on the fifteenth day, the rash of measles appeared.

In a second case, he injected 5 c.c. of a mixture of blood in ascites broth subcutaneously into a healthy person. On the eleventh day, the temperature rose. On the thirteenth day, there was some cough. During the fourteenth night, the eruption of measles developed.

Anderson and Goldberger [2] inoculated monkeys intracerebrally and intraperitoneally with blood from human patients with measles; and on the eleventh day after the injection, there was a rise of temperature, but there was no rash.

These investigators [3] filtered blood from patients with measles and injected the filtrate into monkeys. On the tenth day after inoculation, there was a rise in temperature, and on the fifteenth day, measles developed.

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* Received for publication, Dec. 7, 1923.

1. Hektoen, Ludvig: Experimental Measles, J. Infect. Dis. **2**:238-255, 1905.
2. Anderson, J. F., and Goldberger, Joseph: The Period of Infectivity of Blood in Measles, J. A. M. A. **57**:113 (Sept. 11) 1911.
3. Anderson, J. F., and Goldberger, Joseph: The Nature of the Virus of Measles, J. A. M. A. **57**:974 (Sept. 16) 1911.

Tunnicliff [4] cultivated a micrococcus from the blood of fifty patients in the preeruptive stages of measles.

Blake [5] inoculated monkeys with nasopharyngeal washings, and after from six to ten days, symptoms of measles developed.

Tunnicliff and Moody [6] gave a series of monkeys, guinea-pigs and rabbits intratracheal injections of washings from the nose and throats of patients with measles in the early stage, and obtained mild reactions.

A careful search of the literature does not reveal a case in which the blood from a patient having measles was injected into the blood stream of another person and produced measles. The following cases are of interest because it appears that measles did occur as a result of transfusion of blood, and an opportunity was presented to observe two cases in which measles was transmitted from the mother to the infant. Both cases were on the service of Dr. E. J. Huenekens in the pediatric service of the Minneapolis General Hospital.

REPORT OF CASES

Case 1.—Baby H., girl, aged 9 months, was admitted to the hospital, March 21, 1923, because of swollen glands, otitis media, fever and loss of weight. Her condition did not improve under treatment, and as she could not retain her feedings and was steadily losing weight, a transfusion of blood was decided on. Groupings were made, and as it was found that she and her mother were in Group II, the mother was chosen as the donor. The mother appeared to be in good health.

April 4, 1923, in the morning the baby was given a sinus transfusion of 75 c.c. of citrated blood. The red blood cells, April 2, numbered 3,500,000; the lymphocytes, 11,800. After the transfusion, the red blood cells numbered 4,620,000; the leukocytes, 27,500; which can be explained as a reaction following the transfusion. In a few days, the number of leukocytes fell to 7,500, remaining at that level during the remainder of the patient's stay in the hospital. Two days after the transfusion, she was much improved and was able to retain her feedings. The temperature fell to 99.4 F., and remained at that level until April 12, when it rose to 102 F. (by rectum). The fever continued high and, April 17, a rash developed. Koplik spots were present, and a diagnosis of measles was made. The patient was then transferred to the contagious disease service. Bronchopneumonia developed, and she died, April 27.

In seeking an explanation as to why the patient had measles, we learned that, two days after the transfusion, the mother developed the disease. There were no cases of measles at our station. Only relatives of babies were permitted to come into the ward, and they always wore sterile gowns and were not permitted to approach or touch babies not their own, and were not allowed to take their own babies out of the cribs. On the morning the transfusion was given, the mother did not

4. Tunnicliff, Ruth: The Cultivation of a Micrococcus from Blood in Preeruptive and Eruptive Stages of Measles, J. A. M. A. **68**:1028 (April 7) 1917.

5. Blake, F. G.: Measles, Arch. Ped. **38**:90 (Feb.) 1921.

6. Tunnicliff, Ruth, and Moody, W. B.: Experimental Measles by Inoculation of Monkeys, Guinea-Pigs and Rabbits with Green Producing Diplococcus, J. Infect. Dis. **31**:382 (Oct.) 1922.

touch or come near the baby. Her last previous visit was made four days before the day of transfusion. The interval between admission and transfusion was fourteen days. The interval between the transfusion and the appearance of the rash in the baby was thirteen days. The interval between the transfusion and the development of measles in the mother was two days. The interval between the last visit of the mother and the time she developed measles was six days.

It is unusual for babies of this age to have measles. Since there appears to have been no other source of infection, we are justified in concluding that measles was transmitted from the mother to the child through the transfused blood.

Case 2.—Baby V., girl, born Feb. 21, 1923, weight 2,225 gm., was fed by tube. She was sent home March 3, 1923, still fed by tube and weighing 2,200 gm. She was readmitted to the hospital, May 17, because of loss of weight and regurgitation. The family history was negative. The patient was an only child. She was nursed for two weeks only, and then, because of a breast abscess, modified cow's milk was given. She had regurgitated ever since leaving the hospital. Vomiting occurred soon after each feeding and occasionally was projectile in character. The patient, now 3 months of age, was a poorly nourished underdeveloped child. The skin turgor was very poor. Since she did not respond to treatment and continued to vomit and lose weight, it was decided to perform a transfusion. Groupings were made, and it was found that the baby was in Group II and the mother in Group IV. The mother appeared to be in good health, and as there were no signs of disease, she was chosen as the donor.

May 28, the baby was given 60 c.c. of citrated blood through the sinus, at 9:30 a. m.

Before the transfusion was complete, it was observed that she was not doing well. There was a convergent strabismus and some spasticity. She was put to bed and at 11:30 a. m. all symptoms were improved. She took her feedings well during the rest of the day. The rectal temperature was 99 F. The next day, the temperature was 101 F., and was at a normal level until June 10, when it rose to 100 F. Her condition was very good until June 5, when stools became diarrheal in character. This continued June 7 and 8, the stools being normal, June 9.

Nothing of note occurred until June 10, when the temperature rose to 100 F. The next day, the temperature was 101.6 F., and a rash developed. Koplik spots were present, and a diagnosis of measles was made. The patient was transferred to the contagious disease service. The measles ran the usual course, and the baby was returned to our station. The subsequent history was without events, and she was discharged from the hospital in a satisfactory condition, June 29. The laboratory findings during her stay were negative.

Again we sought for a cause of the measles. There were no cases of measles in our station. The patient had been in our station twenty-five days before developing measles. She occupied a crib in a remote corner of the ward. It was evident that she was infected with measles while in our station. The mother made no comment on the child having measles. On questioning, she denied that she had been sick, but later admitted that two days after the transfusion she developed measles and was sick for a week.

Here the interval between admission and transfusion was twenty-five days. The interval between transfusion and measles in the baby was fourteen days. The interval between the transfusion and development of the measles in the mother was two days.

The mother did not come in contact with the baby on the day of transfusion. She had visited it the day before, but did not handle it. The interval between the mother's last visit to the baby and her own illness was three days.

CONCLUSIONS

1. The virus of measles is present in the blood at least two days before the appearance of the rash.

2. Measles may be transmitted through the transfusion of blood.

3. The two cases seem to establish the incubation period at thirteen and fourteen days.

4. It would seem advisable to take a careful history of those who are to be donors for babies and to look for Koplik spots.

RECENT WORK IN ANATOMY, PHYSIOLOGY AND PATHOLOGY OF INFANCY AND CHILDHOOD*

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INFANT MORTALITY

As a result of his studies of infant mortality as shown by church registration in Schleswig-Holstein, Hanssen,[1] in Kiel, shows that in some places infant mortality was formerly lower than it is today. Eichede, with a present population of 2,900, had an infant mortality of 12 per cent. (twelve babies out of every hundred dying during the first year of life) during the period 1677-1722, as against a mortality of 14.5 per cent. for the period 1900-1912. Low rates are commonly ascribed to the wide use of breast-feeding, and the high rates to epidemics, chiefly of smallpox. It is noteworthy that apparently in former centuries the "summer peak" of infant mortality was not in evidence.

It would seem that the factors of rural population and northern climate might enter into these findings, but the overwhelming importance of breast-feeding in a rural population is shown in another study, on present-day conditions in the Austrian Tyrol,[2] among peasants who for many years have enjoyed excellent incomes and have hoarded treasures. Whereas, in Vienna, 9.9 per cent. of all children born in 1920 died within their first year of life, in two typically conservative and old-fashioned provinces with nine tenths of the population peasants, the figures ranged from 20 to 27 per cent. In some villages, a mortality of from 40 to 50 per cent. was found, and in the richest rural district of Austria, with a population of 767,000, the average was 27.6 per cent. (One child was born dead for each thirty-nine born alive.)

The main reason for this excessive death rate among infants was found in the custom of artificial feeding. This is practiced from lack of knowledge of the importance of breast-feeding, and because of immemorial custom, and carried on without knowledge of the simplest hygienic principles.

For America (registration area of the United States, population 70,000,000), the published birth and infant mortality rates show a birth rate of 24.3 per thousand population (a low record death rate of 11.7 per thousand), and a record low infant mortality rate (death during the first year of life) of 76 per thousand or 7.6 per cent. The corresponding figures for the preceding years were 23.7, 13.1, and 86, respectively—

* Received for publication, Dec. 7, 1923.

1. Berlin Letter, J. A. M. A. **80**:1396 (May) 1923.
2. Vienna Letter, J. A. M. A. **80**:569 (Feb.) 1923.

8.6 per cent. Of the states, Oregon showed an infant mortality rate of 5.1 per cent. and Delaware, 9.8 per cent., and of the cities of 100,000 population or more, Portland, Ore., 5.0, and Fall River, 11.4 per cent.[3]

The death rate of mothers from childbirth in the birth registration area (nine states and the District of Columbia) for 1921, as compiled by the Bureau of the Census,[4] was 6.5 to each thousand live births. Previous rates were: 1915, 6.1; 1916, 6.2; 1917, 6.3; 1918, 1919, and 1920, high, owing presumably to the prevailing influenza which took a heavy toll of pregnant women. The ratio of death from childbirth to the number of women bearing children was about 1 to 150.

The lowest death rate, in this territory, from causes due to childbirth was 5.3 for each 1,000 live births (Connecticut), and the highest, 9.8 (South Carolina). The highest rate for white mothers was 7.8 (South Carolina), and for colored mothers, 14.8 (Kentucky).

The 1921 maternal death rate, 6.5 per thousand live births, when recorded as a percentage death rate, gives 0.65 per cent. for live births.

Since not all infants are born alive (and some births are twin births, and so on), a somewhat different rate is to be expected when the maternal death rate is figured in percentage of the total number of women delivered. Also, in hospital practice, at least as commonly conducted at the present time, the disproportionate number of difficult and pathologic cases may be expected to overbalance the advantages of hospital care for the more normal cases.

Hendry[5] reports a maternal mortality of 1.21 per cent. in a series of 6,982 deliveries in a hospital in the course of eight years. Eclampsia and pneumonia each caused (approximately) 20 per cent. of the deaths; septicemia, complications attending cesarean section, and rupture of the uterus, each 10 per cent.; shock, pulmonary embolus and placenta previa, each 5 per cent.; other causes completing the list.

Greenhill,[6] has reviewed the gross mortality among 10,000 parturient women (Chicago Lying-In Hospital), and found a rate of 0.39 per cent.; i. e., thirty-nine cases in all, twenty of them in primiparae and nineteen in multiparae. The causes of death in these thirty-nine cases were: puerperal sepsis (septicemia) and shock, each six cases; pneumonia and embolism, each four cases; toxemia and cardiac decompensation, each three cases; and coronary thrombosis, status lymphaticus, and pulmonary edema, each one case.

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3. J. A. M. A. **79**:1345 (Oct. 14) 1922.
4. J. A. M. A. **79**:2172 (Dec. 23) 1922.
5. Hendry, W. B.: Maternal Mortality, Canadian M. A. J. **13**:252 (April) 1923.
6. Greenhill, J. P.: Maternal Deaths Among Ten Thousand Parturient Women at Chicago Lying-In Hospital, Surg. Gynec. & Obst. **35**:614 (Nov.) 1922.

One notes in this series the absence of eclampsia, rupture of the uterus, placenta previa and cesarean section as causes of maternal death.

Holland [7] asserts that complications of labor account for 51 per cent. of fetal deaths, the postmortem evidence consisting, as a rule, in cerebral or visceral hemorrhages. In half the cases, he says, the tentorium cerebelli has been torn. Of dead fetuses, after normal breech delivery, this condition has been found in 88 per cent. It has been taught that delivery of the after-coming head should be hurried for fear of pressure on the cord. If, however, death in such presentations is commonly due to a too rapid and forcible molding of the head, better practice, says Holland, would allow the head more time, even as much as ten minutes, if necessary.

The importance of syphilis as a cause of neonatal death has long been known; and its prominence in hospital statistics was emphasized by Williams several years ago.

In a study of the effect of treatment on pregnant syphilitic women and on the life of the child, Williams [8] has recently analyzed the histories of ninety-six treated women (113 pregnancies). Only nine pregnancies ended in abortion and six in premature labor; and, in all these, it seemed permissible to assume that syphilis played no part in the unfruitful outcome. Four infants were born dead or died during the puerperium, and showed signs of congenital syphilis. Of the ninety-eight children remaining, four died from accidents of labor—one premature separation of the placenta, one prolapse of the umbilical cord and two craniotomies—the necropsy in no instance revealing signs of syphilis.

In the 113 pregnancies in syphilitic women, ninety children were discharged from the clinic in apparently good condition. It proved possible to trace eighty of these children: seventy-one were well and gave a negative Wassermann reaction; four could not be tested owing to parental objection, but seemed well; three children had died from pneumonia and one from gastro-enteritis, and one syphilitic child was found.

A review of the maternal data shows that almost ideal results follow anything like efficient treatment of syphilitic women and that surprisingly good results sometimes follow what in men or nonpregnant women would ordinarily be regarded as altogether inefficient treatment. It would seem that there must be something about the pregnant condition which mitigates the virulence of the disease and predisposes to spontaneous cure.

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7. Holland, E.: Intranatal Deaths, Brit. M. J. **2**:588 (Sept. 30) 1922.

8. Williams, J. W.: Influence of Treatment of Syphilitic Pregnant Women in Incidence of Congenital Syphilis, Bull. Johns Hopkins Hosp. **33**:383 (Nov.) 1922.

INFANT FEEDING

Figures presented by Vaughan,[9] recently, led the editor of *Hygeia* to proclaim that "during the summer months cholera infantum is the cause of death of more babies than any other disease" and that Dr. Vaughan's data "are undoubted proof that in about six cases of seven the death can be traced to the mother's inability or voluntary failure to nurse her child."

The Children's Bureau of the U. S. Department of Labor insists that, when the importance of the subject is considered, statistical evidence of the relative influence of artificial and breast feeding in infant mortality seems surprisingly meager, most of the data relating to foreign cities or districts.

Data obtained by the Bureau on the mortality of more than 22,000 live-born infants in eight representative cities of the eastern United States, and extending from birth to the first birthday, show that artificial feeding as actually practiced in typical American city populations is associated with an infant mortality between three and four times as high as the mortality among breast-fed infants.[10] The relation appears in all nationalities and in all income groups, though with variations, depending probably on particular conditions prevailing in the groups. If the first nine months was considered, rather than the first year, artificial feeding was accompanied by a five-fold death rate as compared with breast feeding. The ratio was higher (6.3:1) in the group with earnings of $1,250 and over.

An interesting comparison with these figures would be afforded by impartially collected data from the practice of well-trained pediatricians.

Dietrich,[11] of Los Angeles, has analysed 1,000 cases of infant feeding seen almost consecutively in private practice drawn from the American middle class. He found 37 per cent. of infants were nursed three months or less, and 40 per cent., eight months or more. Nine per cent. of the mothers deprived their infants of breast milk within eight days of birth.

In only 8.4 per cent. of the cases in this series were complemental feedings advised and given. Where complemental feedings were given, breast feeding was usually continued another three to five months.

Modified cow's milk (without the addition of a proprietary food) was used as the artificial or substitute feeding in 72 per cent. of the cases. If certain cases in which goat's milk was given are included, 75 per cent. of the infants in the series were started on milk without proprietary foods.

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9. Vaughan, V. C.: Hygeia **1**:145 (June) 1923.
10. Woodbury, R. M.: The Relation Between Breast and Artificial Feeding in Infant Mortality, Am. J. Hygiene **2**:668 (Nov.) 1922.
11. Dietrich, H.: An Analysis of a Series of Case Records Relative to Certain Phases of Breast Feeding, J. A. M. A. **79**:268 (July 22) 1922.

The remaining 270 infants were fed as follows: on condensed milk, 105; milk and Mellin's food, 42; goat's milk, 36; malted milk, 29; milk and Eskay's food, 27; Dryco, 9; other condensed milks 9; Dennos, 8; Nestle's, 6; peptogenic, Allenbury's, and Mammala, 2; Klim, malt soup, Sunbright, each 1.

Rearrangement of these figures shows that 756 infants were started (early or later) on cow's milk or goat's milk, with, no doubt, usually the addition of water and sugar in some form; 114 on condensed milk; 75, or more, on cow's milk with the addition of cereal derivatives (Mellin's, Nestle's, Eskay's, etc.); and approximately 29 on malted milk, and 12 on dried milk (Dryco, Klim, Mammala, etc.).

Years ago Dr. Holt,[12] writing of "infant foods," said: "They add little or nothing to our resources in infant dietetics; in fact, they tend to retard rather than to advance our knowledge of the subject." And recently it has been said: "There is a science of infant nutrition and a few simple foods, such as sweet and sour milk, with curds and sugar, comprise the entire useful armamentarium." Marriott[13] holds that the indications for the use of these are simple and readily understood by any one; and that the apparently brilliant results from various unusual and complicated formulas can always be explained on the basis of the underlying principles and could have been accomplished just as well by simpler means.

The reasons given for weaning, as ascertained in 337 of the 371 cases in which the infants were weaned during the first three months, as tabulated by Dietrich,[14] yield the following figures: insufficient milk, 69; poor milk, blue and watery, 35; insufficient gain, 29; acute illness of mother, 26; green stools and "bad stools," 26; milk dried up, 18; nervousness of mother, 10; abscess of breast, 9; bad milk—poison milk, 7; menstruation, 7; death of mother, tuberculosis of mother, weakness of mother, cracked nipples, and vomiting, each 6; inverted nipples and child's refusal to nurse, each 5; refusal of mother to nurse, not having nursed previous children, toxemia in mother, operation on mother, pregnancy, each 4; prematurity, and inability to nurse, were given as a reason twice, as was cleft palate; and pylorospasm, once. Other infrequently assigned reasons made up a total of fifty reasons advanced for weaning in 1,000 cases seen almost consecutively in private practice.

When rearranged, these data for 337 cases give the following approximate and very suggestive figures: insufficient milk, "poor milk," and insufficient gain, given as reasons for weaning in 132 cases; acute

12. Holt, L. E.: Diseases of Infancy and Childhood, D. Appleton & Co., New York, 1911.

13. Marriott, W. McK.: Teaching of Infant Feeding, Southern M. J. **15**:530 (July) 1922.

14. Dietrich, Henry: Footnote 11, p. 269.

illness in mother, 26; bad stools, 26; abscess of breast and "poor milk," 16; death of mother, tuberculosis, weakness of mother, pregnancy and cleft palate, 23.

In other words, more than one third of the babies were weaned before three months, and about two fifths of these were weaned for reasons having to do essentially with the quantity of the breast milk; one fifth as many more because of supposedly significant, or significant, faults in the appearance of the stools, and one fifth because of acute illness in the mother.

The importance of more general and careful study of complementary feeding is emphasized. Nor should slight apparent abnormalities in the stools of a breast-fed infant be regarded as equal in significance to changes in the stool of the bottle-fed.

Another mortality report, among artificially fed babies, averaging between three and four times that among breast-fed babies, is found in the report of the Children's Bureau on a study (in Baltimore) of the influence of industrial employment of mothers on infant mortality.[15] Previous reports have shown a definite relation between income and infant mortality. This newer study, based on larger numbers, shows that, even in the same income group, the mortality rate is higher for babies when mothers are employed outside the home.

Among the babies included in this study, the mortality rate for the first year of life was one and a half times the rate among babies of mothers not employed. A much larger proportion of the infants were artificially fed when the mothers were employed away from home, and the mortality among these was between three and four times that among breast-fed babies.

A small family income (father earning $450 or less) led to 29.2 per cent. of the mothers in these families being gainfully employed away from home during pregnancy, and 22.1 per cent. during the infant's first year of life. When there was a larger income (father earning $1,200 or more), 1.2 per cent. of the mothers worked out during pregnancy and 0.6 per cent. during the infant's first year.

Employment of the mother during pregnancy was associated with a higher stillbirth rate (more than twice as high), a higher premature rate (6.2 per cent. of the live births, as against 5.7 per cent.), and a higher mortality for the first month of life (77.3 per cent., as against 39.9 per cent.).

Nearly 40 per cent. of the employed mothers worked until within two months of confinement, and 25 per cent. until within two weeks of confinement.

In evaluating the data obtained in studies of this kind, it is obviously difficult to separate the effects of industrial employment, as such, from

15. J. A. M. A. **80**:948 (March) 1923.

the results of lower family or group intelligence (measurable in some part by the lower earning power of the father), and squalor and indifference.

Rott [16] sees a significant reduction in the percentage of deaths from intestinal diseases in infants, due to the fact that during the war more infants were breast fed.

Bailey [17] writes that in order to prevent premature births the care of the prospective mother must include a reduction of her manual work during the last month of pregnancy, and insistence on a dietary composed largely of carbohydrates.

As a preventive of the high death rate in the neonatal period, he suggests that in maternity hospitals the new-born be turned over to the pediatrician.

Waldstein,[18] in an exhaustive review of the problem of voluntary birth control, considers the number of births and miscarriages reported in the years 1860-1915. In Germany and Vienna, there was a drop in the absolute number born. If miscarriages are considered, it is found that statistics extending over seventy years (commenced by Hegar and Bumm in Germany) show that at least 10 per cent. of all pregnancies terminate in abortion. Study of a series of from 600 to 1,000 or more women indicates that during the twenty-five years of fecund life (from 20 to 45) each woman was pregnant every four years. Waldstein contends that it is natural selection (miscarriage and infant mortality) that tends to keep down the number of individuals.

Hellmuth and Wnorowski [19] show from extensive material that the differences in weight of the new-born at different seasons do not exceed limits covered by statistical work.

Schlossmann,[20] in a study of 13,803 infants in eighteen years, does not find any marked influence of season.

Smith and Merritt,[21] by successive weighings of nursing infants, find that they get the greater part of their feeding of breast milk in the first few minutes, from 40 to 60 per cent. in the first two minutes and from 60 to 80 per cent. in the first four minutes; and that this holds true whether the supply is abundant, moderate or scanty. It is sug-

16. Rott: Mortality of Infants During the War, Klin. Wchnschr. **1**:381 (Feb. 18) 1922.

17. Bailey, H.: Application of Metabolism Studies of Fetal and Neonatal Periods of Life, Am. J. Obst. & Gynec. **3**:591 (June) 1922.

18. Waldstein, E.: Birth and Miscarriages, Wien. klin. Wchnschr. **36**:131 (Feb. 15) 1923.

19. Hellmuth and Wnorowski: Seasons and Weight of the New-Born, Klin. Wchnschr. **2**:75 (Jan. 8) 1923.

20. Schlossmann: Influence of Vitamin A on Weight of New-Born, Klin. Wchnschr. **2**:304 (Feb.) 1923.

21. Smith and Merritt: Rate of Secretion of Breast Milk, Am. J. Dis. Child. **24**:413 (Nov.) 1922.

gested that there is no good reason why a bottle feeding should not be taken in about the same time.

Bakwin [22] has studied the initial loss of weight in new-born babies, correlating weight changes, skin elasticity and serum protein concentration (plasma water). He finds that usually a marked loss of weight in a new-born baby is accompanied by a loss of skin elasticity and an increase in the serum concentration (indicating a diminution in skin and plasma water), though other babies, despite relatively large weight losses, show no evidence of dehydration of the skin or plasma (presumably owing to a high water reserve in the tissues at birth). Again, impairment of skin elasticity often occurs without increase in plasma concentration, and vice versa. Also, the plasma water percentage may increase even though there is no increase in weight.

Cowie [23] would simplify artificial feeding of infants by allotting an ounce of sugar to each day's feeding and, regarding all sugar as 120 calories per ounce, deducting this from the total calory needs (weight in pounds × 45) and supplying the remaining calories from milk (at twenty-one calories per ounce of 4 per cent. milk). For example, a 10-pound infant would require 450 calories: 120 supplied by the sugar, leaving 330 to be supplied by 15½ ounces of milk. Water is added to give the desired bulk. In actual handling of a case, cereals and vegetables are necessary after the eighth month.

Levy [24] asserts that even in the first three months a more concentrated (two-thirds) milk is better tolerated than milk which has been diluted to one-half. He bases his opinion on a study of 195 cases.

Epstein [25] describes his experiences in giving from one to three teaspoonfuls of porridge daily to infants who required complementary food, or to combat constipation. It proved very satisfactory. The stomach, it is said, contracts around the more solid food, and thus prevents swallowing of air and explosive contractions, which lead to vomiting. The advantage of giving a food less fluid than milk to infants with habitual vomiting seems established.

The use of boiled butter (Lowenbury), butter-soup (Brown and others), butter-flour mixtures (Gismondi) and butter-flour pap (Ernberg) are the subjects of other papers.

Variot [26] declares that infants brought up on sweetened milk evaporated at 50 C. develop normally, other things being equal; and

22. Bakwin, I. H.: Dehydration in Newly-Born, Am. J. Dis. Child. **24**:497 (Dec.) 1922.

23. Cowie, D. M.: Simple Practical Method for Feeding Infants, Michigan State M. J. **22**:10 (Jan.) 1923.

24. Levy, J.: Dilution of Milk in Infant Feeding, Deutsch. med. Wchnschr. **48**:1578 (Nov. 24) 1922.

25. Epstein, B.: Porridge in Infant Feeding, Jahrb. f. Kinderh. **98**:85 (April) 1922.

26. Variot, G.: Comparative Values of Condensed Milks, Bull. et mém. Soc. méd d. hôp. de Paris **46**:838 (May 26) 1922.

that his experience with 5,000 infants shows that scurvy need not be feared with this form of feeding. Unsweetened condensed milks are heated to too high a point.

Luttinger [27] urges the use of honey for sugar in infant feeding. It is in largest part fructose (levulose, a levorotatory monosaccharid), rapidly absorbed, and less easily decomposed. It loses its laxative effect on boiling. It has a protein content, from pollen. Luttinger uses it in marasmus, rickets, scurvy and malnutrition; and his experience in more than 400 cases leads him to plead for its more general use.

Clark and Collins,[28] after a study in Boston for the United States Public Health Service, "to determine the safety, usefulness and comparative value of dried milk powder in infant feeding on a practical community-wide basis," say that powdered milk, and especially the whole milk powder, can be safely used for feeding infants when a good grade of fresh cow's milk cannot be obtained. Commercial processes of drying milk are not necessarily destructive of vitamin C, but the use of fruit or vegetable juices is wise.

Poulsson [29] concludes that fat-soluble vitamin A may be administered to breast-fed children through the mother. In a case described, the infant's growth seemed to be arrested at the age of 6 weeks. When the mother began taking a tablespoonful of cod liver oil, three times a day, the infant began to thrive. The mother's milk had always had a normal fat content.

Davison [30] declares that if yeast has any real value in causing an infant to gain in weight, it should be in feeding patients who are convalescent from acute intestinal indigestion or infants suffering from nutritional disturbances such as chronic intestinal indigestion (celiac disease), or physically retarded children. However, feeding yeast (from one-fourth cake to one-half cake a day) to nine infants for from eight to twenty-three days, was without good effect, and in some of the patients abdominal distention occurred, and the stools became frequent.

Rosenstern and Lanter [31] present evidence that the form of solution, the scale of dispersion of the elements of a food rather than its chemical composition, may be of decisive importance in its action on the bowel. In a study of the behavior of crystalloids, colloids, suspensions and

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27. Luttinger, P.: Bee's Honey in Substitute Infant Feeding, New York Med. Rec. **116**:153 (Aug. 2) 1922.

28. Clark, T., and Collins, S. D.: Dried Milk Powder in Infant Feeding Pub. Health Rep. **37**:2415 (Oct. 6) 1922.

29. Poulsson, E.: Fat-Soluble Vitamin A, Norsk Mag. f. Laegevidensk. **84**:35 (Jan.) 1923; abstr., J. A. M. A. **80**:812 (March 17) 1923.

30. Davison, W. C.: Failure of Yeast Therapy in Feeding Infants, Am. J. Dis. Child. **24**:339 (Oct.) 1922.

31. Rosenstern, J., and Lanter: Physical Properties of Food, Ztschr. f. Kinderh. **32**:316 (May 15) 1922.

emulsions, they show that colloids and fine suspensions seem to check diarrhea. Albumin (albumin milk and buttermilk) checks diarrhea, both by its physical and by its chemical properties, while sugar, both physically and chemically, promotes diarrhea.

The length of time which food ordinarily remains in the digestive tract of infants has been studied by Kahn,[32] who concludes that it varies between four and twenty hours, with a usual duration of fifteen hours. The duration is as a rule briefer in breast-fed than in bottle-fed infants. Ordinarily, the figures for the large and small intestines are about the same.

In the prematurely born, the passage averages twelve hours; in dyspeptic babies, from six to ten hours. The difference in passages of shorter duration is chiefly due to more rapid emptying of the small intestine.

BIRTH INJURIES

The various ill-effects to the infant incident to premature and normal birth received considerable attention in the literature of the past year. Hess[33] designates as premature all infants who are born before the end of the normal term of pregnancy (forty weeks), though in common usage the term refers only to those whose gestation period was 260 days or less. He would place in practically the same category congenitally diseased infants, the weaklings, infants born at term, or nearly at term, who have suffered more or less severely during their intra-uterine existence through factors which interfered with their nutrition, and consequently, with their development. He notes the frequent need of orthopedic treatment in these cases.

The low coagulation point and prolonged bleeding time observed in the blood of premature and other new-born infants is emphasized in recent writings.

Munro and Eustis[34] propose the following etiologic classification of cases of intracranial hemorrhage in the new-born: (*a*) traumatic group; (*b*) "asphyxia" group; (*c*) fetal disease group. They would base the diagnosis of intracranial hemorrhage in the new-born on the result of the following determinations: (*a*) history and physical examinations; (*b*) measurement of intracranial pressure by spinal manometer; (*c*) determination of the coagulation and bleeding times.

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32. Kahn, W.: Ueber die Dauer der Dormpassage im Sauglingsälter, Ztschr. f. Kinderh. **29**:321 (July) 1921; Weitere Mitteilungen über der Dauer der Dormpassage im Sauglingsälter, Ztschr. f. Kinderh. **33**:48 (July) 1922.

33. Hess, J. H: Premature Infants, J. A. M. A. **79**:552 (Aug. 12) 1922.

34. Munro, D., and Eustis, R. S.: Diagnosis and Treatment of Intracranial Hemorrhage in New-Born; Report of Fourteen Treated Cases, Am. J. Dis. Child. **24**:273 (Oct.) 1922.

Rosamond [35] thinks a universal routine determination of the blood coagulability would reduce the mortality of the new-born practically 50 per cent., and would probably prevent a large number of cases of birth palsy. Of seventeen cases of convulsions in the new-born seen by him in twelve months, fourteen manifested delayed bleeding-clotting time and were in all probability due to cerebral hemorrhage. One case, in a baby delivered by cesarean section, was marked by absence of all external bleeding; severity of the convulsions, with a duration of thirty-six hours before efforts to stop the hemorrhage were made, and their prompt cessation when bleeding was stopped. The thirteen other cases all responded promptly to blood therapy.

Munro and Eustis would have the treatment of intracranial hemorrhage due to hemorrhagic disease depend on (*a*) the successful etiologic classification of the case and (*b*) the recognition and measurement of the intracranial pressure; and the treatment consists in the administration of normal whole blood subcutaneously until bleeding and coagulation time have returned to normal, and then appropriate relief of the intracranial hypertension.

It will be recalled that Rhodda's method of testing the coagulation time in the new-born consisted in part in placing a drop of blood between two watch crystals and rolling a lead shot through the drop till the shot was caught by the coagulum. He found that the average coagulation time in new-born infants was seven minutes, and ranged from five to nine minutes. He noted that the coagulation time was progressively prolonged till the fifth day, and then returned to normal by the tenth day. Clinically, most spontaneous hemorrhages of the new-born occur in this interval, from the second to the eighth day.

Falls,[36] using essentially the technic of Howell, that his results might be better compared with the figures obtained by others, found that fetal blood at birth clots with normal firmness and rapidity, so that subsequent hemorrhagic tendencies cannot be detected from coagulation tests at this time. At the time of birth, maternal and fetal blood have practically the same coagulation time; and in general the coagulability of the blood of women before, during and after labor, as measured by the estimation of the coagulation time, calcium, and prothrombin content is well within the limits of normal blood coagulability. Use of anesthesia was without effect on coagulation time.

Schwartz,[37] in examining cadavers of infants, found typical focal processes in the brain in 130 infants less than 5 months old, and diffuse

35. Rosamond, E.: Intracranial Hemorrhage in New-Born; Case Report, Southern M. J. **15**:618 (Aug.) 1922.

36. Falls, F. H.: Coagulability of the Blood During Pregnancy and in the New-Born, J. A. M. A. **79**:1816, 1922.

37. Schwartz, P.: Birth Traumatism of Brain, München. med. Wchnschr. **69**:1110 (July 28) 1922.

pathologic changes in 100 others. In 65 per cent. of all new-born dying within five months, he found effects of birth trauma: hemorrhage and softening that could be discerned with the naked eye. His observations led him to believe that the pathology and pathologic anatomy of earlier infancy are determined mainly by injuries to the central nervous system.

Siegmund [38] emphasizes the injury to the vascular system in birth trauma. Mechanical injuries to small vessels, in his view, cause disturbance in the circulation, stasis, and diapedesis of erythrocytes, with impairment of nutrition in adjacent tissue, and resulting degeneration that may lead to necrosis. He states that small foci of softening are found in infants, especially in the premature, within the first six months, and that the fatty degenerative process of neuroglia, known as encephalodystrophia of the new-born, is in the majority of cases due to birth trauma.

Cruickshank [39] reports on a series of 200 mature infants. Hemorrhage was found in about 80 per cent., and gross hemorrhages in 50 per cent., two thirds of which were gross meningeal hemorrhages—and in two thirds of these again, the meningeal hemorrhage was the only gross hemorrhage present, while in the remaining third there were gross visceral hemorrhages also. In approximately one infant out of eight in this series, there was gross visceral hemorrhage without meningeal hemorrhage.

In 200 premature infants (born during the eighth or ninth lunar month of pregnancy), the incidence of hemorrhage was 66 per cent., and of gross hemorrhage, 40 per cent. Gross meningeal hemorrhage alone was less common, being more often associated with gross visceral hemorrhage; and gross visceral hemorrhage alone occurred more than twice as often in mature infants.

A much smaller series of neonatal deaths is reviewed by Capen.[40]

Cameron and Osman [41] state that, among cases of infantile diplegia or paraplegia, it is possible to recognize a group in which the defect is confined to the sensorimotor cortical areas; that since education at first proceeds almost entirely by sensorimotor paths, there is, in early childhood, a deceptive appearance of gross mental defect; later, progress may be rapid and recovery almost complete. Incoordination may remain, and voluntary movements may be stiff and awkward, though character and intelligence may be on a high plane.

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38. Siegmund, H.: Birth Injuries and Their Consequences, München. med. Wchnschr. **70**:137 (Feb. 2) 1923.

39. Cruickshank, J. N.: Hemorrhages of New-Born, Lancet **1**:836 (April 28) 1923.

40. Capen, N. B.: Intracranial Trauma in the New-Born, J. Obst. & Gynec. **29**:572, 1922.

41. Cameron, H. C., and Osman, A. A.: Late Results of Meningeal Hemorrhage of the Newly-Born, Brit. Med. J. **1**:363 (March 3) 1923.

Shoemaker [42] reports an instance of hemorrhagic disease of the new-born, with notes on successful treatment. Bleeding began on the third day, with vomiting of much bright red blood, followed by passage of dark blood and clots by bowel. Loss of blood recurred at intervals through three days, causing the infant to become cyanotic and cold, and the respirations shallow to imperceptibility. As a result of his experience, Shoemaker concludes that calcium lactate is of practically no value in this emergency; that thromboplastic serum, in any of the commercial forms accepted by the Council on Pharmacy and Chemistry, acts promptly as a hemostatic agent if used in sufficiently large doses (in this instance, 10 c.c. was used); that it should be followed, whenever possible, by whole blood transfusion, without loss of time. In his case, whole blood from the father was given by direct transfusion, from the median basilic vein into the longitudinal veins of the infant through the anterior fontanel.

Losee [43] thinks the clinical picture of cerebral hemorrhage in the new-born is usually sufficient to establish a definite diagnosis, and that lumbar puncture will determine the diagnosis sometimes in doubtful cases. The value of lumbar puncture in draining blood from the subarachnoid space depends on conditions; the success of the operation for decompression depends on the location and extent of the lesion. He reports sixteen cases of hemorrhage of the new-born treated by blood transfusion. Eight had been earlier treated with normal human serum without any result, and in one, the hemorrhage occurred after blood transfusion. There were seven cases of subcutaneous hemorrhage; three of cerebral hemorrhage following operative delivery; three of hemorrhage from the umbilicus; two with gastro-intestinal hemorrhage, and one from the wound following circumcision.

Ballance [44] reports a case of difficult forceps delivery with frontal bone fracture and intracranial hemorrhage. An operation was performed on the fourteenth day. A broken fragment had allowed blood to escape from within the cranial cavity to beneath the scalp. The depressed fragment was removed, and the child made good recovery. Six weeks later, no opening in the skull could be detected.

In a consideration of spina bifida and encephalocele, Hess,[45] in saying that the condition is essentially surgical, states that operation may frequently be delayed through frequent paracentesis, with intermittent

42. Shoemaker, J. A.: Hemorrhagic Disease of the New-Born with Direct Transfusion into the Longitudinal Sinus Through Anterior Fontanelle, J. A. M. A. **79**:1608 (Nov. 4) 1922.

43. Losee, J. R.: Hemorrhage in the New-Born, Bull. Lying-In Hosp. New York **12**:100 (July) 1922.

44. Ballance, A. C., and C. A.: Intracranial Hemorrhage in the New-Born; Fracture of Skull of Infant, Lancet **2**:1109 (Nov. 25) 1922.

45. Hess, J. H.: Footnote 33, p. 553.

indications for operation. Hydrocephalus frequently accompanies spina bifida or follows operation.

For the relief of this in cases that have come under his observation, drainage into the subdural space, under the scalp, into the jugular veins, and puncture of the corpus callosum, have given little more than temporary relief. In a series of six cases observed recently, a cylinder of cortex, about three eighths of an inch (0.9 cm.) in diameter, was removed from the frontotemporal region. The plug of cortex extending into the lateral ventricles was removed with a piece of glass tubing having a sharpened edge, after the skull was opened at a lateral angle of the large fontanel and the dura incised and sutured to the arachnoid. The six infants are all living, with no visible evidence of disturbance of sensation or of muscular power. In experimental animals, the defect in the cerebral cortex remained permanent in five out of seven cases, and, in some of them, the lumen was found at necropsy to be lined with epithelium, probably from the lateral ventricles.

It is also stated that paraplegias or diplegias have been reported in more than 3 per cent. of all surviving premature infants; that mental defects in premature infants are, in at least 75 per cent. of all cases, accompanied by spastic monoplegias, paraplegias, or diplegias, and that these figures would be much higher were it not that most of the premature infants suffering from injuries to the brain die very early. Traumatic injuries from labor are seen in a greater percentage of premature infants than of full-term infants. The symptoms are less evident, and roentgenograms should be made in very doubtful cases.

METABOLISM

The metabolism of the new-born has been studied by a number of workers. The problem is a difficult one and seemingly contradictory views are expressed. Where adults have a basal metabolism of approximately 1 calory per kilogram of body weight for each hour, or 24 calories a day, children less than 1 year old may show 50 or 60 calories. In normal recently fed infants, the heat production may reach 60 calories per kilogram a day. New-born infants have been found to have a lower metabolism, perhaps not exceeding 48 calories per kilogram. Difficult questions as to whether the comparisons shall be made on the basis of body weight or body surface enter in. Figures recently obtained by Talbot and his co-workers [46] indicate that the basal metabolism of premature but organically sound babies is startlingly low from any point of view.

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46. Talbot, F. B.; Sisson, W. R.; Moriarty, M. E., and Dalrymple, A. J.: Basal Metabolism of Prematurity. II. Relation of Basal Metabolism to Calorie Intake and Weight Curve, Am. J. Dis. Child. **24**:95 (Aug.) 1922.

This was true in seven of twenty-two premature infants studied by them, who did not gain in weight until they were able to digest approximately 200 calories in the day. A relatively large proportion of the food went to form new body tissue, and less was available for heat production. In the view of these authors, the large excess of the caloric intake over the basal metabolism was necessary because of the relatively great amount of growth essential for the normal development of these babies. Rubner and Langstein (1915) found more than 40 per cent. of the calories ingested as food was retained in prematurely born infants. Talbot and Sisson believe that the amount of heat formed depends on the amount and tone of the active "protoplasmic" tissue, and not primarily on the size of the surface of the body in these infants, and that the active, heat forming, protoplasmic tissues are unable to respond to the excessive heat loss; hence, the subnormal temperature. Talbot's patients did not gain until they were able to digest approximately 200 calories daily, and the only food completely assimilated was human milk.

Hoffa [47] reports other findings. She compared results in normal premature infants given a minimal amount of food with results in others fed abundantly. All were healthy infants of healthy parents. They were fed with pumped breast milk, gradually supplemented with buttermilk. No incubators were used. Many infants were studied, but data are given from eleven cases in the first group and two in the second.

The charts are held to show that, at least in many cases, the actual requirement is less than 100 calories per kilogram. These infants sleep, and scarcely move, and use up very little energy. This physiologic need of rest Hoffa respected by feeding through a stomach tube left in place continuously in the nose, being fastened with adhesive plaster. The milk was slowly increased up to 100 calories per kilogram, and this figure was not overstepped till ten or fourteen days had elapsed without further increase in weight. The growth in weight and length was satisfactory in all. One infant had doubled its birth weight by the twelfth week. All these infants fed on minimal amounts improved with a regularity that was attributed to lack of digestive strain on account of their getting only the nourishment needed, without any excess. Contradictory statements in the literature are explained by the fact that previously congenitally feeble and normal premature infants have been grouped together.

CHILD WELFARE

In a consideration of the basic aims of the child hygiene movement, Veeder [48] groups the methods so far employed under three headings:

47. Hoffa, L.: Requirements in Calories of the Prematurely Born, Arch. f. Kinderh. **72**:6 (Sept.) 1922.

48. Veeder, B. S.: Child Hygiene and the Private Physician, J. A. M. A. **79**:2228 (Dec. 31) 1922.

(1) the use of specific means, as, for example, the crusade for pure milk, or the use of toxin-antitoxin in diphtheria; (2) educational methods, including such diverse items as propaganda through the press, the holding of health exhibits, the teaching of health habits to groups of children in the schools and the visitation of the home by health workers, and (3) the direct supervision of the infant and child by the physician through clinics, or—a better term—welfare conferences.

Veeder finds certain inherent basic defects in the welfare conference. First, experience having shown that the welfare conference must confine itself to the well child, since sick and well children should not mingle and the presence of a sick child attracts a disproportionate share of the attention of the conference, the conference physician is deprived of that observation of the child when sick, which in many instances is the most important factor in determining what to do when the child or infant is well.

Second, the conference physician fails to see the child in its normal, every-day surroundings, and there is a close and intimate relationship between the physical condition of a child and its environment. Attempts to see this environment through an intermediary, a nurse or a social worker, are at best unsatisfactory and incomplete substitutes for personal observation.

Again, there is an element of weakness in the changing personnel of the conference, and in the child's passage from one conference to another as he advances in age.

Finally, welfare clinics are classed as "charities," and limited in their work to the poor; whereas, there is just as much need of health work among the children of the middle and well-to-do classes of society.

In Veeder's opinion, the best results can be obtained only if there is direct and constant supervision of the child through infancy and childhood by one physician, who sees the child in sickness as well as in health, and who has an intimate and personal knowledge of its parents, its home life and daily environment, its play and companions.

Such a man should be the physician in general practice. That he is lacking in knowledge concerning the hygiene and development of normal infants and children is the fault of the physician's training, not of the physician.

However, if the principles and practice of child hygiene are as important as they are believed to be, the situation, in Veeder's opinion, will automatically correct itself in time.

Emerson [49] holds that the forces affecting the child's health which must be coordinated to insure success are: the home, the school and

49. Emerson, W. R. P.: Nutrition and Growth in Children, Boston M. & S. J. **188**:8 (Jan. 4) 1923.

other agencies; medical care, and the child's own interest. Summarized, his program consists of (1) weighing and measuring as a means of identification; (2) diagnosis based on complete physical, mental and social examination; (3) removal of physical defects as a prerequisite for successful treatment; (4) measured feeding (forty-eight hour diet record); (5) midmorning and midafternoon lunches; (6) midmorning and midafternoon rest periods; (7) regulation of physical, mental and social activities to prevent overfatigue (forty-eight hour list of activities); (8) nutrition classes for the treatment of malnutrition; (9) nutrition or diagnostic clinics for problem cases (average weight for height to be used as a minimum standard of nutrition and growth).

In a study of the effect of living conditions on schoolchildren of large cities, Kurcharski (Berlin Letter, J.A.M.A. **79:** 2178 [Dec. 25] 1922.) had a comprehensive questionnaire filled out by more than 1,300 children, belonging mainly to the poorer classes of an outlying section of Berlin. Only 8 per cent. of the children were in a good state of nutrition, 21 per cent. were much undernourished and 16 per cent. were mentally backward, judging from their achievements in school. While it was shown that unfavorable social conditions, such as overcrowded apartments, lack of employment of the father and inadequate care on the part of a working mother, exerted a harmful effect on the mental development of the schoolchildren, it could not be shown that any damage to physical development had occurred as a result of these conditions.

A report of the United States Department of Labor [50] on the children of wage earning mothers (Chicago) covers 2,066 children in 843 families, one fourth of them colored. Overfatigue and illhealth were found in the mothers. In the children, retardation of school progress—more of the children were below the standard grade for their age—was found, and, in some instances, overwork by children who had responsibility for household tasks beyond their strength. Remedial measures are those looking toward reducing the necessity for wage earning by mothers of young childen; i. e., improvement in economic conditions that will make the fathers' earnings more nearly adequate; training of the mothers in household management and the care of children, and preserving the family group through social measures (prevention of accidents, promotion of health, mother's pensions, etc.).

Pearson,[51] as the result of a statistical study, holds that, on broad lines, health and intelligence are innate and are chiefly controlled by inheritance; that health and intelligence are correlated though

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50. Children of Wage Earning Mothers: A Study of a Selected Group in Chicago, Rep. U. S. Dept. of Labor.

51. Pearson, Karl: Draper's Company Research Memoirs, London Letter, J. A. M. A. **80:**1861 (June 25) 1923.

not markedly; that general health changes very little during the whole school period; that it does not seem feasible in the present state of medical knowledge to improve intelligence by modifying health; that it is the intelligent rather than the slow or dull children who exhibit athletic power; that general intelligence and a variety of psychic characters remain unchanged throughout the whole range of school life, and that health is associated only in a minor degree with certain psychic characters.

In a study of elementary grade schoolchildren in a typical American community, Sterling [52] found that the school work had little if any adverse effect on the pupils' weight, and that the under-age child (school entrance here, 6 years) made as good a showing in this respect as the normal age or average child. It is apparent that school life, apart from detrimental influences which may exist in the home environment, is not ordinarily harmful to the child's state of nutrition.

In England, a consultation committee [53] that included Dr. J. S. Adami notes that, up to 1850 or later, it was assumed that the education of girls must be different from that of boys because they belonged to a "weaker sex." Then it came to be held that it should be based on their equality. Now it is coming to be recognized that equality does not demand identity but is compatible with and even depends on a system of differentiation.

The committee recognizes that most boys, especially at adolescence, have a habit of "healthy idleness," and thus can protect themselves against overpressure; whereas girls, being more amenable to authority and more industrious, are more liable to overfatigue, in studies and in sports. It is recommended that the first school examination for girls should be about a year later than for boys; that school physicians and others give more attention to protecting girls against physical fatigue and nervous overstrain, and that, in girls' day schools, in some instances, the amount of home preparation should be reduced, in view of domestic duties.

In a lengthy paper on the mental and physical health of school children, Sanger Brown, 2d.[54] doubts that Goddard's contention (in "Human Efficiency and Levels of Intelligence") that efficiency and success in life are largely dependent on intelligence and that failure is due to a lack of it is exactly the case. Many people with high intelligence do not succeed; while others with inferior intelligence, through their

52. Sterling, E. B.: Nutrition and Education, Pub. Health Rep. **37**:2798 (Nov. 10) 1922.

53. London Letter, J. A. M. A. **86**:414 (Feb. 10) 1923.

54. Brown, Sanger: Mental and Physical Health of School Children, J. A. M. A. **80**:1351 (May 12) 1923.

pleasing personality and adaptability in getting along with people, do relatively well.

He pictures at some length the complex character of the child's education in the preschool years, his acquirement of control of his body, of patience and selfcontrol and of social adaptability. The success with which this early development in physical, mental and social spheres is accomplished is tested, in most cases, when the child enters school.

The great majority of children do reasonably well, he thinks, in the schools of today, but the fact remains that a certain percentage get along indifferently, or not at all. Of this small group, some are physically below par, some acquire slowly, some are remarkably brilliant and some have the makings of genius in them. His observations are based on a survey of 150 of these cases. Such children are usually spoken of as difficult or unusual. At one time, it was thought that mental defect was the basis of most of the difficulty, and reports were made which showed that from 60 to 80 per cent. of the conduct disorders of children were attributable to mental defect. Now, some difficult children are found to be defective; but by no means the majority. Some suffer from malnutrition, but some are perfect physical specimens.

In this survey, nervous symptoms were found in 20 per cent. of the group; epilepsy in four instances, and various nervous symptoms in the others. States of anxiety and fear, night terrors, stammering in several cases, and overactivity were found; also instances of undue sex stimulation before puberty, and nervous instability from undue fear of competition in school.

One third of the group had some type of visual defect, some requiring glasses. A few cases of defective hearing were found, the result of former otitis media. Nearly half had enlarged tonsils, in many cases only slightly enlarged and apparently causing no symptoms; but in a number there was associated difficulty in nasal breathing, with restlessness at night and night terrors, attributable to the interference with free passage of air. In nineteen cases, there was defective nasal breathing; in some, a mild defect caused by a deviated septum.

Poorly nourished children seemed to suffer in a particular way mentally, being emotionally unstable and having nervous symptoms.

For the relief of these children, appropriate medical and social measures are suggested, and particular forms of education. For the nervous ones, class progress is the less important thing until mental stability is gained. In time, the nervous tension subsides, the worried look disappears, sound sleep returns and the ability to concentrate and learn easily. For the children who are slow, yet have no nervous handicaps, but make a low record by psychologic tests, manual education should be introduced at the age of 11 or 12 years, or earlier, and time not squandered on academic studies.

Heller [55] draws attention to children who are intellectually normal or above normal, but who fail in the motor sphere. They are clumsy in dressing, and do not learn to run, jump or dance gracefully. He advocates individual training, devoted toward bringing the child to understand the mechanical details of such movements, training both mind and muscles.

In a study of defects in 15,605 schoolchildren, Bruce [56] found that at 5 years of age, 58 per cent. of the "crippling" was due to rickets of the most pronounced type; 9 per cent., to tuberculosis (pulmonary tuberculosis being conspicuous by its absence); 7.4 per cent., to nervous diseases; 6.3 per cent., to mental deficiency (retardation?); 6 per cent., to chronic bronchitis, and 3.9 per cent., to anemia and malnutrition without symptoms of other disease. The remaining 9 per cent. of crippling was due to eye conditions (mainly strumous ophthalmia), a few cases of heart disease (the acquired ones due to scarlet fever and rheumatism) and miscellaneous conditions such as congenital and acquired deformities. One notes the high percentage of handicapping due to rickets, tuberculosis (other than pulmonary) and chronic bronchitis, in these British schoolchildren of tender age.

In London, Sir George Newman's report (1921) [57] shows that there are 164,000 "exceptional" children. Of these, the blind number 58,000; the feeble minded, 31,000; the cripples (other than the tuberculous), 23,000; tuberculous cripples, 13,000; those having pulmonary tuberculosis, 2,000, and so on.

In contrast with these figures for children, the conditions found in adult life are of interest. General Ireland [58] states that of all Class I men, more than one young man in five was physically unfit to perform any type of military service either at home or abroad.

The more important causes of rejection were: organic diseases of the heart, 11.5 per cent. of the total causes of rejection; tuberculosis, 9.3 per cent.; errors of refraction, 8.4 per cent.; underweight, 7.6 per cent.; mental deficiency, 4.5 per cent.; hernia, 4.3 per cent.; flatfoot, 3.6 per cent.; defective and deficient teeth, 3.2 per cent., and defective speech and hearing, 2.6 per cent. Many of these conditions obviously reach back into childhood. Many must seem relatively unimportant to nonmilitary men.

Of the large classes of diseases, the defects of the bones and organs of locomotion ranked first, with 17.2 per cent. of the total causes of

55. Heller, T.: Motor Underdevelopment of Children, Ztschr. f. Kinderh. **34**:287 (Jan. 10) 1923.
56. Bruce, R.: Defects in School Children, Brit. M. J. **2**:346 (Aug. 26) 1923.
57. London Letter, J. A. M. A. **79**:1700 (Nov. 11) 1922.
58. Ireland, M. W.: Physical Defects Discovered in Selective Draft Men During the World War, J. A. M. A. **79**:1579 (Nov. 4) 1922.

rejection. Diseases of the heart and blood vessels second, 15 per cent.; diseases of the eye third, 12.6 per cent.; and tuberculosis fourth, 9.3 per cent.

Nine men out of each hundred had two defects which were of sufficient military importance to note.

Of these same Class I men, more than two out of every five (i. e. 47 per cent.) had a physical defect of sufficient importance to be noted in the reports of the examinations of the local and camp examining boards. Practically all of these defects were of some importance even to those who did not expect to engage in arduous physical exercise or labor. Of the individual defects which were recorded most frequently in the men examined, the principal ones occurred in the following order: flatfoot, 11.7 per cent.; venereal disease, 5.7 per cent.; hernia, 4 per cent.; refractive errors of the eye, 3.3 per cent.; organic disease of the heart, 3.1 per cent.; underweight, 3.1 per cent.; tuberculosis, 2.5 per cent.; hypertrophied tonsils, 2.3 per cent.; defective teeth, 1.4 per cent., and mental deficiencies, 1.2 per cent.

Vercoe [59] has studied the effect of the child's position in the family on his health, relative intelligence, physique and resistance. In comparison with the first, the second, the third child, etc., in the family, there is no appreciable difference between any of the children investigated. In incidence of disease, the eldest child fares definitely the worst, the eighth and upward the best. As far as his series goes, he concludes that the quality of the average child does not deteriorate in any way with successive pregnancies; and the quality of the family does not deteriorate in any way with increase in quantity, in the environment and class under consideration.

On the other hand, Reiter and Ihlefeldt [60] conclude, from a study of 634 legitimate children, that repeated pregnancies and the higher age of the mother influence the somatic and psychic qualities of the child unfavorably.

Edberg [61] estimates that about 130 cases of harelip or cleft palate appear yearly in the 125,000 children born in Sweden. The condition seems to occur in boys 14 per cent. oftener than in girls. Direct heredity of the deformity seems evident in 2.3 per cent. of cases; coincidence in brothers and sisters in 3.7 per cent., and a combination of deformities in 5.1 per cent.

Some evidence of inheritance is also noted in congenital luxation of the hip joint (more common in girls) and in talipes (more frequent in boys).

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59. Vercoe, R. H.: Effect of Position in Family on Health of Child, Lancet **2**:758 (Oct. 7) 1922.

60. Reiter and Ihlefeldt: Influence of Mother's Age on Development of Child, Klin. Wchnschr. **1**:2524 (Dec. 16) 1922.

61. Edberg, E.: Hare-Lip and Cleft Palate, Acta Chir. Scandinav. **55**:1 (July 15) 1922; abstr. J. A. M. A. **79**:1562 (Oct. 28) 1922.

Rosenstern [62] publishes five cases of children who were much smaller than other children of their age, the lack of height being due chiefly to shortness of the lower extremities, and the mutual proportions of the body corresponding to a younger stage. He speaks of such children as exhibiting temporary dwarf growth. Some of the children change later to normal proportions.

Seham [63] finds that the responses to exercise that are encountered in normal children of school age are those that are encountered in adults. The physical capacity of children, as judged by the maximum physical output, is in direct relationship to age, circumference of chest, circumference of thigh and vital capacity. Height and weight do not alter it so constantly.

Emerson [64] believes that there has been a tendency to overrate the importance of corrective exercises; that most cases of bad posture are due to general weakness of a body with too little weight to support its height, and that the first need is a program that will bring the child up to his normal weight.

NUTRITION

In the absence of satisfactory data from other sources, Holt and Fales [65] have employed the statistical method to ascertain the amount of fat that healthy children are accustomed to consume. While many factors, social, economic and otherwise, may tend in civilized life to modify instinctive cravings, data obtained by this method should at least offer a starting point for further studies.

As a result of their investigation, Holt and Fales conclude that, in general, it seems rational to supply in the diet of the child as much as 4 gm. of fat per kilogram daily at 1 year, decreasing the amount to about 3 gm. per kilogram at 6 years, and maintaining this value throughout the growth period. They feel that there is little evidence that a liberal amount of fat in the diet is harmful to children with normal digestion, and much evidence that fat is an important and necessary component of the diet during the entire growth period. Fat is said to exert a protective action against the irritating effects of the products of carbohydrate fermentation. The authors urge that the grounds for the current impression regarding the harmful effects of fat in children be carefully investigated.

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62. Rosenstern, J.: Temporary Dwarf Growth, Ztschr. f. Kinderh. **34**:310 (Jan. 18) 1922.

63. Seham, M., and Egerer-Seham, G.: Physiology of Exercise in Childhood. I. A Study of Normal Children of School Age, Am. J. Dis. Child. **25**:1 (Jan. 1) 1923.

64. Emerson, W. R. P.: Nutrition and Growth in Children, New York, D. Appleton & Co., 1922.

65. Holt, L. E., and Fales, H. L.: Food Requirements of Children. III. Fat Requirement, Am. J. Dis. Child. **23**:471 (June) 1922.

They assert [66] that a diet in which the percentage distribution of the total calories is fat, 35 per cent.; protein, 15 per cent., and carbohydrates, 50 per cent. is one which meets the nutritive needs of the child after infancy, and is well borne by the digestive system, and hence may be considered as well balanced with respect to these elements.

In studying the carbohydrate intake of 100 healthy children from 1 year to 18 years of age, Holt and Fales [67] found an average figure of 10 gm. per kilogram. It is held that a diet that is excessive in carbohydrates leads to an abnormal deposition of fat without corresponding increase in muscle development; that children taking such a diet have feeble resistance to infection; that a relationship exists between the high proportion of carbohydrate in the modern diet and the prevalence of dental caries, and that definite digestive disturbances, chiefly intestinal, may be produced when the carbohydrate in the diet is excessive—there may result increased fermentation with acid, loose stools or constipation with flatulence and abdominal distention, and when long continued these disturbances are very difficult to control.

In an article of popular character on the accessory food factors, vitamins, Dr. Holt [68] notes how greatly the variety and palatability of our food have been increased by the use of such processes as milling, drying, canning, condensing and sterilizing; also the widened distribution of foodstuffs that is made possible, and the protection against local famine. These preserved foods are of great help in the nutrition of both children and adults, and one would not stop the use of them if it were possible. But the increasing knowledge of vitamins has shown that the procedures involved in their preparation have their disadvantages, and even dangers.

When the nature of these disadvantages and dangers is thoroughly understood and their importance appreciated, the remedy will come also. In the food of infants, it is only vitamin C that is likely to be injured. The amount of this vitamin in milk is very small, at best, and the body evidently has a store sufficient to meet its needs for a considerable time, scurvy appearing usually only after an interval of between five and seven months.

Vitamins C and A are abundantly supplied by milk, eggs, green vegetables and fruits, all of which are expensive foods for the poor, but should be included in a nursing mother's diet; and by yolk of egg, the juice of steamed green vegetables and, best of all, by cod liver oil, for the infant. To infants whose principal or sole food is any one of

66. Holt, L. E., and Fales, H. L.: Food Requirements of Children. V. Percentage Distribution of Calories, Am. J. Dis. Child. **24**:311 (Oct.) 1922.

67. Holt, L. E., and Fales, H. L.: Food Requirements of Children. IV. Carbohydrate Requirement, Am. J. Dis. Child. **24**:44 (July) 1922.

68. Holt, L. E.: Practical Application of the Results of Vitamin Studies, J. A. M. A. **79**:129 (July 8) 1922.

the forms of heated, dried or condensed milk, it would appear quite sufficient if an antiscorbutic were begun at the age of 5 months. In winter time, it would seem a wise precaution to supplement cow's milk, which at that season may be poor in vitamins, with a vitamin-rich food.

Holt has never seen or known of a case of scurvy in a child over 2 years of age under normal peace conditions. As to vitamin A, so indispensable for the growth of children, it is necessary only that care be taken that the diet include an ample supply, since it is not likely to be injured in the preparation or preservation of food.

Children should eat a variety of food. Special dangers may follow the habitual use of a very restricted diet. During the entire period of growth, the diet should include, if possible, whole milk, or if skim milk is used, it should be supplemented by butter. Of the butter substitutes, those which contain beef fat, mutton fat and peanut oil are better than those in which vegetable oils or lard are important constituents.

A diet which contains no milk whatever should contain ample amounts of the leafy or green vegetables. The chief objection to cabbage, a rich source of all the vitamins, and cheap, and lettuce and celery, when used in the raw state, is the difficulty of making children masticate them properly.

Cereals, particularly those from whole grains, and potatoes are important and adequate sources of vitamin B.

Fruits have other uses than as laxatives and as sources of mineral salts, and should form a regular part of the diet. When fresh fruits are not available, dried fruits may be given, but they are distinctly inferior to canned tomatoes as sources of the antiscorbutic vitamins.

If the daily diet contains a reasonable amount of unskimmed milk, cereals, potato, green vegetables and fruit, one need not fear a vitamin deficiency.

The place of purin in the diet of children is discussed by Czerny [69] in a paper on natural immunity in children. An infant gets along very well on a food poor in purin. At what age a diet rich in purin must be introduced is a matter of controversy. There are, he says, no doubt, children who will thrive for years on a diet poor in purin, and there are a good many children who need food rich in purin from the time they are 2 years old. The highest susceptibility to disease, combined with a marked tendency to hyperplasia of the lymphatic tissue, is seen in children who subsist for long periods on food poor in purin. As research in metabolism has shown that not every child is able to extract from primitive forms of food all that his organism needs, it is necessary to prescribe food elements in definite known forms, or harm may arise.

69. Czerny, A.: Natural Immunity in Children, Klin. Wchnschr. **1**:561 (March 18) 1922.

Blatherwick and Long,[70] in studies on urinary acidity, find that the drinking of large amounts of orange juice results, in young women, in the production of alkaline urines, an increased organic acid excretion and a decreased ammonia content of the urines. It was not possible to overreach the organism's ability to oxidize citric acid even though the amounts drunk in one day were the equivalent of about 48 gm. of acid.

The drinking of large amounts of lactic acid milk caused the formation of strongly acid urine, the increased acidity being due to the excretion of increased amounts of acid phosphate, as indicated by simultaneous increase in the titratable acidity and phosphorus. The lactic acid appeared to have been completely oxidized or retained, as there was no change in the organic acid excretion.

In a study of the effect of proteins on bacterial fermentation, Rühle[71] confirms Kayser's and Bluhdorn's observation of increased formation of acid in the presence of proteins. He finds that the figures are still higher if products of peptic-tryptic digestion are used, the stronger fermentation being simply due to a physicochemical binding of acid with the proteins, which enables the micro-organisms to continue the fermentation and produce more titrable acid; but for the same reason this acid does not hurt the mucosa of the intestine, and thus, proteins have no harmful effects in intestinal fermentation.

Buckheim[72] reports findings in roentgen-ray examination of the gastro-intestinal tract in children over 1 year of age, twenty-three cases, and quotes from the literature. On the average, the stomach empties in two hours, and the small intestine in from two to four hours.

Sauer, Minik, and Alexander[73] have studied further the gastric findings in children with anorexia. Some years ago, it was pointed out that one of the pronounced effects of delayed emptying time of the stomach in children is loss of appetite, and that a child will not be hungry with a portion of a previous meal in the stomach.[74] (One must except here certain healthy growing children who seem always to be hungry.)

In this work with underweight children, the authors occasionally encountered children who were free from tuberculosis, anemia, physical defects, diseased tonsils, adenoids and other known causes of anorexia,

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70. Blatherwick, N. R., and Long, M. L.: Studies in Urinary Acidity. I. Some Effects of Drinking Large Amounts of Orange Juice and Sour Milk. J. Biol. Chem. **53**:103 (July) 1922.

71. Rühle, R.: Proteins and Bacterial Fermentation, Jahrb. f. Kinderh. **100**: 127 (March) 1923.

72. Buckheim, I.: Roentgen Examination of Alimentary Tract, Arch. f. Kinderh. **72**:81 (Nov. 18) 1922.

73. Sauer, L. W.; Minik, L. D., and Alexander, W. G.: Gastric Findings in Children with Anorexia, J. A. M. A. **79**:184 (July 15) 1922.

74. Kerley, C. G.: New York J. M. **20**:345 (Nov.) 1920; cited by Sauer.

yet who when given three meals a day, avoiding excess of fats, ate less than the required number of calories, and were underweight because they ate insufficiently. A study was made of the gastric motor and secretory functions in twenty-one such children and twelve normal children. A meal recommended by the Royal Society of Medicine for roentgenographic examination of the alimentary canal was employed. It was given within fifteen minutes, and serial films were made four hours later, and each succeeding hour until the stomach was emptied. Other details as to ingestion, posture and occupation were supervised. Observations were repeated after a few days in a number of subjects in both groups, and in most subjects after a lapse of several months.

It was found that the stomachs of all twelve children with good appetites emptied within five hours, with an average emptying time of four and one-half hours. For the twenty-one children with poor appetites, the time was six and one-tenth hours.

The average total hydrochloric acid for the children with good appetite was 61.2, the free acid 26.3; for eighteen with poor appetite, the total acid was 49.4, the free acid 14.9.

A relation between these functions and hyposthenia or asthenic habitus was noted. Remedial measures proved helpful.

Chievitz [75] has studied the hydrochloric acid secretion in fifty-three infants after a barley gruel test meal. No instance of congenital achylia was discovered, but there was achylia or hypochylia in almost half the cases of essential digestive disease.

In healthy infants, the values of the free hydrochloric acid averaged 8 (Günzberg), 11 (Congo) and 14 (phenolphthalein).

TETANY

Recent studies on tetany deal chiefly with the blood chemistry of the condition. Freudenberg and György report the successful use clinically of ammonium chlorid.

Elias [76] reminds us that a therapeutic influence of acid or alkali does not prove anything as to the etiology of any disease; in this case, tetany. He maintains that disturbances in the acid-alkali metabolism are not essential for tetany, that the phosphoric acid ion seems to have a special function, in very small doses, of increasing the irritability of the nerves, and that its amount in the blood is increased in tetany.

Hess and Lundagen [77] studied (1921) the phosphate content of the blood of about sixty infants, making monthly examinations by the Bell

75. Chievitz, I.: Hydrochloric Acid in Infants, Acta Pediat. **1**:416 (April 15) 1922; abstr., J. A. M. A. **79**:88 (July 1) 1922.

76. Elias, H.: Relations of Acid and Alkali to Tetany, Wien. klin. Wchnschr. **35**:784 (Oct. 5) 1922.

77. Hess, A. F., and Lundagen, M. A.: A Seasonal Tide of Blood Phosphate in Infants, J. A. M. A. **79**:2210 (Dec. 30) 1922.

and Doisy method. The infants were from 6 to 18 months of age, living under good hygienic conditions, and were on a diet of certified raw milk or of dried milk, receiving the usual amount of orange juice, and (the older ones) cereal.

The plotted findings show a steady seasonal decrease from about 4 mg. in December to a low point (about 3.50 mg.) in March, and then a rapid increase as summer approached (4.50, etc., in June). The phosphate tide was not intimately dependent on the variety of milk fed. The authors are unable to state what the condition may be in breast-fed infants, save that 50 per cent. of well nourished breast-fed infants attending an outpatient department had been found to show clinical evidence of rickets at the end of March, and it seemed probable that they likewise were susceptible to seasonal fluctuations. In older children, the variations were less marked; but in ten children, aged from 2 to 3 years, the rise was definite in every case. In adults, the phosphate content was found to be lower and more stable.

An earlier investigation showed that, in infants, the inorganic phosphates of the blood could be raised to the normal level by frequent exposure of the child to the sun's rays. Later, it was shown that the same result could be accomplished with irradiation with the carbon arc lamp. It seemed probable that the ultraviolet rays were the ones concerned. Comparison of the present curves with meteorologic data for the same period shows a suggestive relationship in the increasing amount of sunshine and daily mean elevation of temperature.

After foreshadowing the existence of a (less marked) seasonal calcium tide, the authors proceed to the generalization that this seasonal variation evidently indicates that the chemical constitution of our blood is not constant for all periods of the year; that this probably holds true for other tissues and that this may exert an influence on general nutrition, growth and resistance to infection.

Greenwald [78] opposes the view that tetany is due to an alkalosis, or increase in the hydroxyl ions in the blood. As tetany following the removal of parathyroids seemed relieved by injections of acid, it was thought an alkalosis existed and was overcome by the acids. This has seemed supported by the fact that tetany has been observed after intravenous administration of alkali, soda bicarbonate solutions, etc. Also gastric tetany has been explained on the assumption that the loss of acid in the gastric juice left a surplus of base in the blood.

According to Greenwald, tetany, instead of being due to alkalosis, is attributable to a high concentration of sodium in the blood. Experimentally produced convulsions are ascribed to "sodium poisoning," a

78. Greenwald, I.: Supposed Relation Between Alkalosis and Tetany, J. Biol. Chem. **54**:285 (Oct.) 1922.

disturbance of the normal equilibrium between sodium and other ions. Even in tetany of hyperpnea, it is not the alkalosis per se but the tissue anoxemia resulting from the increased stability of oxyhemoglobin that is held to be the exciting factor.

Cruickshank [79] writes that there is a loss of calcium in parathyroid tetany, and that in severe cases the diffusible calcium may amount to 94 per cent. of the total calcium—normally from 60 to 70 per cent.; that the immediate state of alkalosis is not necessarily marked, and with the development of the signs of severe tetany passes rapidly into a condition of acidosis, as shown by a steadily falling p_H of the blood. He adds that the calcium deficiency and the great loss of colloidal calcium are merely indicative of a rapid protein disintegration.

Tisdall and Harris [80] have determined the concentration of phosphorus in forty-five normal persons ranging in ages from 4 months to 44 years, and find that the inorganic phosphate content of normal serum from birth to 20 years is remarkably constant (practically always above 5 mg. per hundred cubic centimeters. At this age, it drops sharply to a lower concentration, and is again remarkably constant at this lower level throughout adult life (below 4 mg. per hundred cubic centimeters.

The drop in phosphate content of the serum at the age of 20 corresponds to the period of cessation of bone-growth. During the period of union of fractures in adults, the phosphate content of the serum is raised to a level approximately the same as that present in childhood; i. e., the period of active bone growth. These findings are presented by the authors in a most striking manner in a graph.

Hamilton,[81] in an extended study on the calcium and phosphorus metabolism of four prematurely born infants, writes that everything tends to show that infants born at term are provided with a surplus of calcium which is lacking in the prematurely born, and found that the calcium intake of his subjects was evidently inadequate to meet their metabolic demands. The author asks whether treatment directed toward correcting an assumed calcium deficit might not ward off rickets and other pathologic conditions common to the prematurely born.

In a clinical case of obstruction of the stomach, in an adult, Grant [82] found the plasma carbon dioxid capacity greatly increased, the blood chlorids markedly decreased and the serum calcium in the upper limits of normal.

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79. Cruickshank, E. W. H.: Experimental Tetany, China M. J. **36**:445 (Nov.) 1922.

80. Tisdall, F. F., and Harris, R. I.: Calcium and Phosphorus Metabolism in Patients with Fractures, J. A. M. A. **79**:884 (Sept. 9) 1922.

81. Hamilton, B.: Metabolism of Prematurely Born Infants, Acta Pediat. **2**:1 (July 31) 1922; abstr., J. A. M. A. **79**:1562 (Oct. 28) 1922.

82. Grant, S. B.: Tetany: Report of Cases with Acid-Base Disturbance, Arch. Int. Med. **30**:355 (Sept.) 1922.

Tisdall,[83] on the other hand, believes the sodium-calcium ratio to be the important factor in the production of tetany, with the exception of the gastric type, in which the disturbance appears due to an increase of the bicarbonate ion. He says no evidence has been found that the calcium-phosphate ratio has any influence on the production of tetany.

On the therapeutic side, Freudenberg and György[84] report that by giving ammonium chlorid from 3 to 7 gm. a day, internally, to spasmophilic infants, they were able to banish the symptoms of tetany and check the mechanical and faradic hyperexcitability. Ammonium chlorid is pleasanter to take than the necessary doses of calcium chlorid (from 6 to 8 gm.) and more acceptable to children. Its effect is only symptomatic, it is said, but immediate danger is averted, and time is gained for employing cod liver oil and quartz lamp irradiation, to bring about permanent change.

THE THYMUS

Hammar[85] presents a lengthy publication on the thymus gland. During his studies over a period of more than twenty years he has investigated the thymus in nearly 300 normal and 500 pathologic cases. He finds that the thymus is never normal after death from disease or in extreme inanition. His microscopic analysis of the thymus in thirty-seven cases of sudden death in children, from internal causes, which might be classed as "thymus deaths," showed that the thymus was of normal size and apparently normal structure in all but five. He finds the thymus is not a transitory organ but functions up to old age. He says the Hassell's corpuscles seem to present the essential functional changes and form the morphologic expression of antitoxic activity. None of the evidence as to an internal secretion from the thymus is conclusive. At puberty, the parenchyma begins to be reduced, but this age involution does not check the antitoxic action of the gland. Roentgen irradiation disintegrates the lymphocytes, and for a time the thymus is changed to a purely epithelial organ.

HEART AND BLOOD VESSELS

Raeder[86] reports an instance of congenital malformation of the heart, associated with anisopia, and with curious branching of the vessels of the aortic arch, occurring in the infant of a primiparous woman, 40

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83. Tisdall, F. F.: Influence of the Sodium Ion in the Production of Tetany, J. Biol. Chem. **54**:35 (Sept.) 1922.

84. Freudenberg and György: Ammonium Chlorid in Tetany, Klin. Wchnschr. **1**:410 (Feb. 25) 1922.

85. Hammar, J. A.: Function of the Thymus, Upsäla Läkaref. Förh. **27**:147 (Aug. 5) 1922.

86. Raeder, O. J.: Congenital Malformation of the Heart, with Complete Obliteration of the Pulmonic Artery, J. A. M. A. **79**:16 (July 1) 1922.

years of age. The presence of small nodules in the valve cusps of the tricuspid valve offered support, as an alternative view to an argument for inflammatory causation (fetal). The anomalies were: complete obliteration of the pulmonary artery at its origin from the right ventricle; perforation of the intraventricular septum; patency of the ductus arteriosus which functioned from birth until death (ninth day); hypertrophy of the right ventricle; presence of an open foramen ovale and of an aortic arch giving origin to a single large branch, which immediately divided into four branches of approximately equal caliber; dilation of the aorta and displacement of its origin to a position almost directly over the malformed intraventricular septum and the presence of small nodules, some of them dark colored, on the mitral and tricuspid valves. The views of various writers on the etiology of such anomalies are given.

An instance of acute infantile endocarditis is described by Skinner.[87] The patient was a 4 months old infant that suffered from an intractable eczema, but otherwise appeared remarkably well. The infant was admitted to the hospital and about fifteen hours later died quietly in his sleep. No symptoms were observed that suggested a cause of death. At necropsy, lesions were found only in the heart and lungs.

On the surfaces of both lungs were several bluish marks about the size of a mustard seed, which on closer examination proved to be minute subpleural hemorrhages. The heart appeared normal in size and color, but the mitral valve was gravely involved, the free edges and auricular surfaces of the cusps being covered with a growth of soft vegetations, not large and quite recent, shining and pink in color and extremely friable. No congenital defects of any kind were present. There was no evidence of pulmonary infarction or cerebral thrombosi. The coronary arteries appeared patent. Skinner thought the most likely explanation of the sudden death lay in the onset of ventricular fibrillation consequent on the presence of an embolus in a coronary artery, sufficiently small to have passed beyond the openings.

Hutchison[88] reports a case of aneurysm of the ductus arteriosus in a girl, aged 6 years, who died from sudden and profuse hemoptysis. The child had not been well since an attack of measles five months earlier, followed by diphtheria and then by "pleurisy." On admission, she complained of pain in the left side of the chest with cough and feverishness. There was a soft systolic murmur at the apex and over the sternum. There was some dulness in the left infraclavicular and suprascapular regions, with diminution of the breath sounds and some

87. Skinner, E. F.: Case of Infantile Acute Endocarditis, Lancet **1**:1147 (June 10) 1922.

88. Hutchison, R.: Case of Aneurysm of Ductus Arteriosus, Brit. J. Child. Dis. **19**:85 (April-June) 1922.

crepitation over the right apex in front. The temperature ranged from 100 to 101 F.; the dulness at the left apex became more pronounced as the case progressed, and the apex beat extended further to the left. The short systolic murmur disappeared. Necropsy disclosed a rupture of an aneurysm of the ductus arteriosus into the lung.

An instance of stenosis of the portal vein in a boy of 6 years is reported by Bardach.[89] In early infancy, there had been a suppurative dermatitis with abscesses. At 2 years, there had been a brief period of vomiting of blood, and at 4 years, epistaxis and swelling of the joints. The child had always been pale, and had always refused to eat green vegetables and fruit. Otherwise, he had seemed well.

The presence of a large spleen, severe anemia and profuse hemorrhages in the digestive tract were explained at necropsy as being the result of stenosis of the portal vein. The vein had become imbedded in cicatricial tissue from old peritonitic changes (referable to the suppurative dermatitis of infancy), and stenosed. The splenic vein showed thrombosis, the bleeding came from varices in the digestive tract.

Huber and Koessler,[90] in a study of the pathology of bronchial asthma, state that, even in the purely allergic asthma of a 16-month-old infant (at that age already showing a definite thickening of the bronchial wall, as compared with a well infant of the same age), the exudation into the bronchi and bronchioli, with complete obstruction, is proof of combined action of the exudative and bronchiomuscular systems in the production of stenosis. These observations made it plain to them that, in man at least, the allergic reaction of the tissues is not confined alone to the smooth muscle fiber system, but involves also the whole organ system which serves exudative processes, endothelium, epithelium, capillaries and glands. The paper is well illustrated.

An instance of bilateral cystic kidney in a girl of 3 years, with symptoms of renal insufficiency, dating from 8 months, is reported by Greene.[91] A convulsion at 8 months was perhaps the first of a series of uremic attacks. Albumin was present in the urine throughout the whole period of the disease, and the amount increased during uremic attacks, but was never large. The specific gravity of the urine varied between 1.005 and 1.012; casts were absent and no Bence-Jones or protein body

89. Bardach, M.: Stenosis of the Portal Vein in a Child, Arch. f. Kinderh. **71**:270 (Aug. 26) 1922.

90. Huber, H. L., and Koessler, K. K.: Pathology of Bronchial Asthma, Arch. Int. Med. **30**:689 (Dec.) 1922.

91. Greene, C. H.: Bilateral Hypoplastic Cystic Kidneys: Report of a Case Simulating Chronic Diffuse Nephritis, Am. J. Dis. Child. **24**:1 (July) 1922.

other than serum protein was demonstrable in the urine. Death was due to uremia, with starvation acidosis as a contributing factor.

The postmortem picture was that of bilateral hypoplasia of the kidneys with cyst formation. The renal tubules were characterized by marked cystlike dilatations, especially on the proximal convoluted tubules. There was no evidence of obstruction, and the dilatation was apparently secondary to functional hypertrophy of the tubules.

An instance of fetal teratoma, the size of an orange, involving the left ovary, in a girl of 6 years and 10 months, is reported by German.[92] He states that the age of the patient is the chief point of interest, as the condition seems to have been reported in only one younger patient (3½ years of age), the next being 11 years old.

In German's case, abdominal symptoms followed a fall over a small rocking chair, and at operation, three weeks later, when there was a leukocyte count of 23,350, an inflamed appendix was found, and a tumor the size of a large orange, blackened and with a twice-twisted pedicle, involving the left ovary. Both were removed. The tumor, a dermoid cyst, contained portions of a fetus, including hairy scalp, a part of the upper jaw, and six teeth, such as those of a 3-year-old child.

Sironi and Sabatini[93] report on a series of twenty cases of enuresis in children. In sixteen, the fifth lumbar vertebra was deformed or there was spina bifida, and in one case, the fifth lumbar vertebra and the sacrum had separated. The authors suggest that such findings indicate that an anatomic basis for enuresis is not rare. They comment on contradictory publications as to malformations, occult spina bifida and the like, as factors in enuresis.

Rivers[94] reports twenty-three new cases of influenza meningitis and reviews the records of 197 other cases. Seventy-nine per cent. of the cases occurred in patients under 2 years of age. The mortality in the 220 cases was 92 per cent. Of the seventeen patients who recovered, twelve were 2 years of age or older.

From the case records, it is possible to say that the meningitis might have been primary in the majority of instances. The disease is produced by a group of influenza bacilli which are closely allied culturally and serologically. Treatments of various kinds have been used, but as far as can be determined, none has accomplished much.

Mackey and Garrod[95] report a case of congenital porphyrinuria and pink teeth, an extremely rare inborn error of metabolism, and give a

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92. German, W. H.: Fetal Teratoma in a Child, J. A. M. A. **79**:2000 (Dec. 9) 1922.

93. Sironi, L., and Sabatini, L.: Essential Enuresis in Children, Riv. di clin. Ped. **20**:399 (July) 1922.

94. Rivers, T. M.: Influenzal Meningitis, Am. J. Child. Dis. **24**:102 (Aug.) 1922.

95. Mackey, L., and Garrod, A. E.: Congenital Porphyrinuria, Associated with Hydroa Aestivale and Pink Teeth, Quart. J. Med. **15**:319 (July) 1922.

résumé of the cases previously described. The evidence of congenital onset in their own case, in a 6-year-old boy, is more complete than in other cases. The condition was not familial, and his parents were not blood relatives.

The boy presented the usual association of porphyrinuria and extreme sensitiveness of the superficial tissues to light, as shown by annual eruptions of hydroa aestivale, or vacciniforme, on the exposed surface of his skin. The deep pink coloration of the milk teeth was quite exceptional. Transillumination of the hands afforded strong evidence that the bones were deeply pigmented, and a roentgenogram showed delayed ossification of the carpal bones.

Halbertsma [96] has found records of nine instances in which one of twins presented mongolian idiocy. He analyses them and reports further five similar instances. The twins were of opposite sexes in all but one instance, and a bivitelline pregnancy may be assumed. In two further cases, the sexes were the same, and both twins were of the mongolian idiot type.

These last two cases sustain the assumption of an endogeneous origin. Halbertsma inclines to incriminate the ovum, as the mothers were mostly close to the extreme end of the reproductive period; in his cases 35, 41, 43 and 44 years old.

DIABETES AND INSULIN

In 1910, Osler, in his textbook, stated that diabetes probably accounted for about ten deaths per hundred thousand population, being apparently about as frequent in the United States as in European countries (8.7 per hundred thousand in England and Wales, and in Paris 14, in 1890). In 1911, Holt stated that the disease was a very infrequent one in children, there being but eight cases in children under 10 years of age in Pavy's collection of 1,360 cases, and only one patient under 10 years of age in Prout's 700 cases. Infrequency of urine examinations in children probably accounts in part for these low figures. Stern collected 117 cases of diabetes in children.

DeLange and Schippers (1915) [97] found between 500 and 600 cases of diabetes in children on record and encountered six cases in 10,848 child patients admitted to one hospital, during eleven years. They reported on eight recent patients, aged 2, 4, 5, 6, 8, 11 and 12 years. Joslin and Gray (1917) [98] analysed a series of 123 cases in patients

96. Halbertsma, T.: Mongolian Idiocy in Twins, Nederlandsch. Tijdschr. v. Geneesk. **2**:22 (July 1) 1922; abstr., J. A. M. A. **79**:1561 (Oct. 28) 1922.

97. DeLange, C., and Schippers, J. C.: Diabetes Mellitus in Children, Nederlansch. Tijdschr. v. Geneesk. **2**:785, 1915; abstr., J. A. M. A. **65**:1150 (Sept. 25) 1915.

98. Joslin, E. P., and Gray, Horace: Diabetes in Children, J. A. M. A. **68**:1869 (June 16) 1917.

under 15 years of age; and in a recent report of Joslin's in 127 cases, there were thirty-one under this age. One was 1 year old, and the average age of onset in the thirty-one cases was 7 years.

Thirst, polyuria and wasting have been the more striking symptoms. Unexplained incontinence may be the earliest symptom noted. Other symptoms are dry mouth, scanty perspiration, irregular sleep, furuncles and abscesses, decayed teeth and genital irritation.

The course has usually been rapid; the younger the child, the more rapid the course. The majority of untreated cases have proved fatal in from two to four months from the time the symptoms became sufficiently marked to make a diagnosis possible; few lasted more than five months, though occasional cases of the milder type lasted a year or two.

In few diseases has the prognosis been so bad as in diabetes of children. Some, as Stern, after a study of seventy-seven cases, have held that diabetes in children is hopeless, and all treatment useless. Holt, in 1911, wrote that he had seen no cases fail to terminate unfavorably. The cases of DeLange and Schippers all terminated fatally in from eight or nine months to two years and a few months. In Joslin's hundred and twenty-three cases, the duration of the disease in patients either living or dead at the time of the report averaged 1.1 years. Five patients had gone on eight or nine years, and appeared to be in good health and sugar-free.

The seat of the disease has been recognized as in the pancreas. The older methods of treatment secured some beneficial results and prolongation of life by keeping the patient's nutritive processes at the lowest possible level by forcing on him food that in a round-about way, rather than in a direct way, was ultimately used by the diseased pancreas. Whether anything in the nature of a cure of the disease has ever been approached may well be doubted.

With the discovery of insulin, a new chapter in the history and treatment of diabetes is opened. Ever since Mering and Minkowsky, by surgical experiments on dogs, demonstrated the existence of pancreatic diabetes, attempts at specific pancreatic therapy have been made, but have been uniformly unsuccessful, and are now chiefly of historical interest. It was reserved for Banting and his co-workers, in 1921, to isolate an active, glycolytic, nontoxic pancreatic extract, called by them insulin.

Allen [99] has written an excellent summary of the articles published on this subject up to 1922, presenting the various steps in developing Banting's important discovery. A more recent article by Banting and

99. Allen, F. M.: Summary of Publications on Insulin to Date, J. Metabolic Res. **2**:125 (July) 1922.

others [100] describes the clinical results obtained in diabetics. The insulin which is made in the United States (Iletin-Lilly) has been used extensively in this country during the last few months.

Major [101] describes a case of severe juvenile diabetes. His first photograph (taken Dec. 7, 1922) shows the patient when he had been a diabetic for two years, and it had been impossible to render him aglycosuric except on a diet of 5 per cent. vegetables, with days of complete starvation. His weight had fallen to 18 pounds (8.2 kg.). A second photograph, taken Feb. 26, 1923, after the patient had been under treatment a little over two months, shows him weighing 30 pounds (13.6 kg.) and on a diet containing 55 gm. of carbohydrate, 85 gm. of protein, and 100 gm. of fat. April 15, the child was in excellent condition, weighed 32 pounds (14.5 kg.), and was receiving a diet consisting of 60 gm. of carbohydrate, 80 gm. of protein and 70 gm. of fat.

During a period of three months, the daily dosage of insulin was reduced from 75 to 15 units. This, Major felt, was indication of an increasing tolerance.

Insulin is described as an aqueous solution of an active principle from the pancreas, which affects sugar metabolism. Its administration to man in severe cases of diabetes restores to the body the lost ability to oxidize carbohydrate, and glycogen is again stored in the liver. If the solution is administered (hypodermically) at suitable intervals, the blood sugar is maintained at a normal level, and the urine remains free from sugar. Fat is also burned and, as a result, ketone bodies do not appear in the urine, and diabetic acidosis and coma are averted.

The use of insulin greatly simplifies the diet of diabetic patients. Enough carbohydrate can always be ingested and utilized to supply the normal carbohydrate demand for the complete and proper metabolism of the other food principles desired by the patient (Cowie and Parsons), provided, of course, the demand is not excessive. It permits giving a diet that satisfies the natural, normal cravings of the patient; permits of maintaining a more comfortable weight, and improves the patient's mental attitude.

Yet it is not to be forgotten that the substance is a powerful drug, and an overdose is followed by the development of serious symptoms which demand immediate treatment. If insulin is to be administered without adequate control of the blood sugar, it is safer to have the blood sugar somewhat above normal, with transient glycosuria, than to have the urine sugar-free and the blood sugar at or below normal.

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100. Banting, F. G.; Campbell, W. R., and Fletcher, A. A.: Further Clinical Experiences with Insulin, Brit. M. J. **1**:8 (Jan. 6) 1923.

101. Major, R. N.: The Treatment of Diabetes Mellitus with Insulin, J. A. M. A. **80**:1597 (June 2) 1923.

In babies, it would seem that less danger attends the administration of insulin because the usual method of spacing feedings can be taken advantage of to insure sufficient carbohydrate coming into the blood stream at a time when otherwise the effect of the dose (hyperinsulemia) might cause a dangerous reduction of the blood sugar.

In children who are no longer bottle-fed, danger might easily arise because of the inability of the child to announce developing symptoms. Careful management and suitable spacing of the meals is necessary.

It is to be remembered that insulin is not yet advanced as a cure for diabetes; it is one more means of treatment. All the other means are to be conserved, utilized. The administration of insulin will enable the patient to have carbohydrate so that protein and fat can be added to the diet in sufficient quantities to give him energy to carry on work and to maintain the ordinary economic burdens of life. His diet is rendered appetizing, and life is made more tolerable. It is possible also that the improved general health and the lightening of the burden of work to be borne by the diseased organ may result in regenerative processes setting in.

Whether insulin is to be regarded as by any means a cure for diabetes in children remains to be seen. In some patients, progressively smaller doses of insulin are needed to take care of the excess of sugar in the blood. It may well be that, in time, some of the patients will improve to such an extent as to be able to get along without the drug, and eventually can eat ordinary diet without glycosuria. They may perhaps then be said to be cured.

The interesting point has been made [102] that if the administration of insulin increases the expectation of life (of diabetics) to that of non-diabetics, it will not be long before there will be a greatly increased number of diabetics in the population. This will increase the need for the drug. Collip [103] has recently obtained a substance somewhat similar to insulin from various plants.

Charles Street at Thirty-Fourth.

102. "W. S. T.": Clifton M. Bull. **9**:41 (June) 1923.
103. Collip, T. B.: Proc. Soc. Exper. Biol. & Med. **22**:321.

BOOK REVIEW

LE DISPENSAIRE MARIN. UN ORGANISME NOUVEAU DE PUERICULTURE. By J. JARRICOT, Paris, Masson and Company, 1921.

This rather bulky volume does not carry conviction. The use of sea water in the treatment of infants may be excellent, but we do not feel that the author has proved his point. In discussing his cases, the author does not seem to have used true standards for comparison and, therefore, his conclusions are of doubtful value. For example, he compares the rate of growth of a sick infant, under sea water therapy, with the rate of growth of a normal child of the same age, instead of comparing it with the growth of similar sick infants who had no treatment or who had other standard forms of therapy.

The author repeats himself often, and the book is filled with much extraneous material.